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ANNALS OF
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VOLUME VI APRIL, 1933 NUMBER 10

The Heart in Myxedema*†

Electrocardiograms and Roentgen-Ray Measurements before and after Therapy

By J. LERMAN, M.D., R. J. CLARK, M.D., and J. H. MEANS, M.D., F.A.C.P.,
Boston, Massachusetts

REVIEW OF THE LITERATURE

IN various articles and textbooks dealing with myxedema, very little has been said regarding the heart. The literature covering the subject of the heart in myxedema is marked by paucity, contradiction, and confusion.

In 1918 Zondek[1] introduced the term "myxedema heart" and described its characteristics as follows:

I. Before treatment with thyroid.

1. Dilatation of the left and right heart which may be of a very high degree.
2. Slow, indolent heart action with normal blood pressure.
3. Lowering of the auricular wave and the *T*-wave of the electrocardiogram.

II. Following treatment with thyroid.

1. Return of the heart from marked dilatation to somewhere near normal size.
2. More lively heart action and more rapid pulse without change in blood pressure.
3. Gradual return of the *P*- and *T*-waves to normal.

In this article he reported four cases which showed the above characteristics. An illustration of the roentgen-ray shadow of the heart and measurements were given in one case. The following year he presented two additional cases[2] giving similar results.

Assmann[3] in 1919 reported a confirmatory case. Meissner[4] in 1920 reported three cases of myxedema with cardiac studies before and after treatment. The first case showed the marked shrinkage of 4.5 cm. The second was complicated by chronic nephritis and showed no change in size. The third showed a normal heart before therapy and no change in size following it. Laubry et al[5] reported a

*Received for publication October 22, 1932.

†From the Thyroid Clinic and Metabolism Laboratory of the Massachusetts General Hospital.

case of myxedema in a patient with typical angina and cardiac hypertrophy without valve lesion. There was no response to digitalis but a marked response to thyroid. No cardiac measurements were given.

In 1925 Fahr[6] published the first paper on the heart in myxedema in this country. He stated that in spite of the neglect of the subject of heart failure in myxedema in works on both myxedema and heart disease, he believed that it was a prominent feature of all outspoken cases of myxedema. He added to the picture described by Zondek a negative *Q-R-S* complex in Lead III of the electrocardiogram which disappeared on thyroid administration, showing that it was not due to left ventricular preponderance. He described in detail one case showing a shrinkage of 6.3 cm. in the transverse diameter over a period of seven weeks of treatment. This patient had all the signs of decompensation, including orthopnea, ascites, a large liver, and râles at the lung bases. Previous trial with digitalis for three weeks had given no improvement. The signs and symptoms all cleared under thyroid medication. As a control the patient was taken off thyroid for six weeks and thereupon the size of the heart increased and again was brought back to normal by thyroid. The electrocardiogram at the beginning showed negative T_1 and T_2 and negative Q-R-S_3. These returned to normal in seven weeks.

In 1925 Christian[7] reported 32 cases of myxedema at the Peter Bent Brigham Hospital and stated that "such a change in a heart as pictured in Fahr's case, I have never observed in any form of cardiac disease". Twenty-two of his patients had no suggestion of a cardiac lesion by physical examination or history. Of the remaining 10, two had chronic valvular disease, five had myocarditis, two had hypertension, and three had minor cardiac disturbances. There was no case of notable cardiac enlargement. Unfortunately neither roentgen-ray nor electrocardiographic studies were given.

Willius and Haines[8] reported a study of 162 myxedema patients. From this group 91 per cent showed no signs or symptoms of organic cardiovascular disease. The 9 per cent that did, could be accounted for on grounds other than those of myxedema. They did not mention roentgen-ray examination of the heart in any case. Fifty-five patients had electrocardiograms taken, of which 54 per cent were normal. Twenty-three per cent of the abnormalities disappeared under thyroid. In 23 per cent studies were too incomplete for conclusions. They took the position that the data presented did not justify the establishment of a cardiac syndrome characteristic of myxedema.

Case[9] analyzed 58 patients with myxedema, without finding any to correspond to Fahr's cases.

Means, White and Krantz,[10] in 1926, gaining the impression from Fahr's paper that the cardiac disturbance which he described was of frequent occurrence in myxedema, studied 48 cases of myxedema seen in the Thyroid Clinic of the Massachusetts General Hospital in the twelve previous years. The nearest approach to Fahr's case was one showing moderate enlargement and a shrinkage of 2.3 cm. over a two-week period of treatment.

The electrocardiogram showed an inverted T_2 which returned to normal under treatment. They concluded: "Myxedema heart, in the sense of Zondek and Fahr, is far from common. On the other hand we are not prepared to join those who feel that it does not exist. The evidence presented by Zondek and Fahr of a marked cardiac dilatation rapidly subsiding under thyroid seems incontrovertible, and our own case in a less striking way is one in point."

Thacher and White[11] that same year studied the electrocardiographic findings in 14 cases. All of these showed low T-waves, that is below 2 mm., or inverted T-waves, pulse rate average of 68, P-waves present in every case, but often small, and Q-R-S complexes of low potential which in some cases increased, as did the T-waves, with thyroid. There was no abnormal axis deviation and no auriculoventricular or intraventricular block. The P-R interval was less than 0.18 second except in one case where it was 0.20 second. There was considerable parallelism between the height of the T-waves and the level of basal metabolic rate. Thacher and White concluded that myxedema results in an abnormal and more or less characteristic electrocardiogram corrected by thyroid therapy.

From this same clinic, Sprague and White[12] reported that hypothyroidism was a common cause of low voltage in the electrocardiogram. Of the 57 cases studied, myocardial failure from arteriosclerosis accounted for 34 and hypothyroidism for 10. The low voltage of the latter disappeared in those cases reacting favorably to thyroid medication.

Also in 1926 Zins and Rösler[13] reported a case of myxedema heart and cardiac insufficiency in a woman of 47, being reduced 3.3 cm. after three weeks of thyroid. Schittenhelm and Eisler[14] presented a case with reduction of 3.3 cm. in the heart size along with return of small P-waves and negative T-waves to normal.

Fahr[15] returned to the subject in 1927 with a review of his first case and five additional cases of large hearts shrinking with the taking of thyroid. The cases were well substantiated with roentgen-ray findings (table 1). He says, "Willius and Haines' conclusions are very hard to understand. With the largest material of myxedema cases in the world they have been unable to find a single case of cardiac failure attributable to myxedema, whereas in other clinics where the amount of material is very much smaller, numerous cases of heart failure, unquestionably due to the same factor as the myxedema, have been found. In the past four years we have seen just six cases of myxedema at the General Hospital and the University Hospital. All six cases showed more or less heart failure, the symptoms and signs of which receded partially or completely on thyroid medication." In three of his six cases such signs of cardiac failure as râles at the bases, big liver, and ascites were observed. In the other three, edema, dyspnea, etc., could be part of the myxedema picture without postulating cardiac failure.

From the Washington University Clinics[16] in 1929 came the report of a case of myxedema with cardiac decompensation which disappeared under thyroid medication. In a period of six

weeks the heart decreased in size 3.5 cm. The electrocardiogram showed all T-waves inverted before treatment with T_2 and T_3 becoming normal and T_1 diphasic after six weeks.

Holzman[17] gave a good review of the situation and reported a case with marked cardiac enlargement (transverse diameter of heart 19.7 cm., and of chest 30.5 cm.). Electrocardiogram showed left axis deviation, low voltage and flat T_3. In seven weeks the basal metabolic rate had risen from minus 20 to plus 9. The heart was narrower by 1.7 cm., but this change was attributed to the different positions of the diaphragm. The electrocardiogram remained unchanged. This patient had a myxedema history of twelve years' duration, and the author suggests that this may have produced a true hypertrophy rather than dilatation.

In 1930 Ziskin[18] reported one case with a change in the transverse diameter of 1 cm. after four weeks of treatment. The electrocardiogram showed diphasic T_1 and T_2 and delayed P-R interval. The T-waves returned to normal with treatment. Davis[19] reported a case from Fahr's clinic with a shrinkage of 6.2 cm. in six weeks. This patient also showed low T-waves and a P-R interval of 0.2 second, all of which returned to normal. Tung[20] reported one case showing a shrinkage of 2.2 cm. in transverse diameter of the heart. He followed the electrocardiograms of seven patients, which showed low P- and Q-R-S waves, and inverted and flattened T-waves. These returned to normal after thyroid medication. Recently Ayman, Rosenblum, and Falcon-Lesses[21] reviewed the literature and reported two of their own cases. They found decreases in the size of the heart and return to normal of small or flat P- and T-waves with treatment.

Reid and Kenway[22] studied the electrocardiographic changes in 260 cases of low metabolic rate, five of which had genuine untreated myxedema. They found that there was no change characteristic of low rate, but that myxedema showed the typical changes described by others: low P- and T-waves and small Q-R-S complexes. They comment upon the fact that those who have found cardiac changes as first described by Zondek have not reported more than a small number of cases. This study made them aware of the great necessity of carefully distinguishing myxedema cases from simple low rate cases, and they suggest that insufficient distinction between these two may in itself account for the diversity of opinion regarding myxedema heart.

We have summarized in tables 1 and 2 all of the known cases of myxedema in the literature which have data regarding the heart size and electrocardiogram.

Thus we have seen that complete reports of the size of the heart in myxedema have been made in relatively few cases. Most of these were published because of a strikingly large heart or marked response to thyroid. Nowhere has any number of cases been reported as a series giving the findings of the size of the heart before and after treatment. Possibly changes in the size of the heart and in the electrocardiogram take place in many treated cases of myxedema. Conse-

TABLE I
CASES REPORTED WITH ROENTGEN-RAY MEASUREMENTS OF HEART

Author	Transverse Diameter before Treatment	Transverse Diameter after Treatment	Shrinkage	Time
	cm.	cm.	cm.	
Zondek[1]	19.7	14.0	5.7	8 weeks
Assmann[3]	16.7	12.7	4.0	3 "
Meissner[4]	20.0	15.5	4.5	—
Means et al[10]	14.0	11.7	2.3	16 days
Zins and Rösler[13]	14.9	11.6	3.3	3 weeks
Schittenhelm et al[14]	18.0	14.7	3.3	—
Fahr[6,15]	19.0	12.7	6.3	7 "
	16.0	12.3	3.3	5 "
	15.2	11.7	3.5	5 "
	14.4	13.0	1.4	5 "
	13.0	11.9	1.1	10 "
	18.2	15.9	2.3	5 "
Holzman[17]	19.7	18.0	1.7	2 months
Wash. Univ. Clinics[16]	22.0	18.5	3.5	6 weeks
Ziskin[18]	14.0	13.0	1.0	4 "
Davis[19]	19.0	12.8	6.2	6 "
Tung[20]	15.0	12.8	2.2	—
Ayman et al[21]	13.1	12.0	1.1	7 "
	14.0	11.3	2.7	9 "

TABLE II
SUMMARY OF ELECTROCARDIOGRAPHIC REPORTS IN THE LITERATURE

Author	No. of Cases	Findings before Treatment	Findings after Treatment
Zondek[1,2]	6	Low P- and T-waves in all cases	Normal
Fahr[6,15]	1	Negative T_1 and T_2; negative Q-R-S_3	Normal
	1	Inverted T_1, flat T_2	Normal
	1	Flat T_1	Normal
Means et al[10]	1	Inverted T_2	Normal
Thacher and White[11]	14	All low T_3; several with low complexes	All normal
Wash. Univ. Clinics[16]	1	Inverted T-waves	T_1 diphasic; T_2 and T_3 normal
Holzman[17]	1	Left axis deviation; low voltage; flat T_3	No change
Reid and Kenway[22]	5	All low P- and T-waves; 3 with low Q-R-S	Normal
Willius and Haines[8]	55	54% normal; 23% changes in T and Q-R-S; 23% incomplete studies	All normal
Ziskin[18]	1	Diphasic T_1 and T_2; delayed P-R interval	T-waves normal; P-R interval unchanged
Davis[19]	1	Low T-waves; P-$R = 0.2$ sec.	Normal
Tung[20]	7	Low P and Q-R-S; inverted and flattened T-waves	Normal
Ayman et al[21]	2	Small or flat P- and T-waves	Normal

quently it appeared desirable to study the heart in a large series of patients with myxedema before and after treatment. Such a study would have the additional advantage of giving us statistical data for purposes of comparison with similar studies in other diseases.

Method and Material

With these things in mind we began a systematic study of the heart in myxedema about three years ago. Being especially interested in the size of the heart, we tried to obtain a teleoroentgenogram before treatment and one or more after treatment with thyroid. About half of the patients included belong to a group whose treatment started before the beginning of this study but who had had measurements of the heart and electrocardiograms taken before treatment. These patients were recalled and the cardiac studies repeated.

All but one of the cases reported are patients who were studied in the hospital and had repeated metabolism tests done. They were carefully separated from cases of simple low metabolic rate showing no clinical evidence of myxedema. Cases of postoperative myxedema or cases where there was any question regarding the diagnosis were excluded. Any case of luetic or rheumatic heart disease was excluded, but cases with possible hypertensive heart disease were included.

Roentgen-Ray Studies

The available teleoroentgenograms were remeasured and those taken before and after thyroid compared with special reference to the position of the diaphragm, rotation of film, and similarity of points of measurement. Special attention was also paid to the internal diameter of the chest. Assuming that a larger diameter on the repeat plate indicates a greater degree of inspiration, then the diaphragm may be assumed to be at least as low or lower than in the first plate. Since a low diaphragm gives an apparent decrease in heart size and a high diaphragm an apparent increase, it was necessary to repeat the roentgen-ray examination of the heart in several instances on account of the position of the diaphragm. It may be noted that in table 3, the chest diameter of seven cases is found to be more than 0.5 cm. greater in the teleoroentgenograms after thyroid medication than in the one before medication. However, only two of these cases (E. J. and J. W.) belonged to the group with a significant change in the size of the heart. Direct comparison of the plates for any given case showed very little variation in the position of the diaphragm. In only one instance (R. M.) was the diaphragm of the repeat plate lower by a whole space than in the first plate. It is therefore correct to state that errors due to position of the diaphragm did not play an important rôle in these cases.

In table 3 are given the complete cardiac measurements in 30 patients with myxedema, before and after treatment with thyroid extract. A total of 86 teleoroentgenograms is recorded. Table 4 summarizes the changes in the size of the heart and in the blood pressure as a result of treatment. Both tables are arranged in the order of the degree of shrinkage in the transverse diameter of the heart.

TABLE III

MEASUREMENTS OF THE HEART IN 30 PATIENTS WITH MYXEDEMA BEFORE AND AFTER THYROID MEDICATION

Initials	Right	Left	Trans. Diam.	Length	Base	Half Diam. Chest	Time Interval*
Mrs. N. C.	6.5	12.8	19.3	18.0	11.9	13.0	
	6.2	11.9	18.1	16.8	10.7	12.7	12 days
	3.2	9.2	12.4	13.6	7.6	12.8	6 months
Mr. R. M.	6.8	14.0	21.4	19.8	12.6	15.8	
	4.2	11.5	15.7	11.5	11.7	16.0	6 weeks
Mrs. B. S.	4.7	11.8	16.5	16.8	12.1	13.2	
	3.5	10.1	13.6	15.1	9.2	13.3	3 weeks
	4.9	6.5	11.1	14.0	9.2	12.6	2½ months
	3.3	8.1	11.4	13.1	10.8	12.8	8½ months
Mr. E. J.	5.3	14.1	19.4	17.9	11.5	14.7	
	5.0	12.8	17.8	17.4	10.7	14.8	10 days
	3.7	13.2	16.9	17.1	9.6	14.6	3 weeks
	3.5	12.0	15.5	17.5	11.7	15.3	5 months
Mrs. J. P.	5.9	8.7	14.6	13.8	9.9	11.5	
	4.1	7.1	11.2	12.5	10.1	11.4	2 weeks
	3.5	7.8	11.3	13.0	9.5	11.1	5 weeks
Mrs. L. C.	4.2	9.9	14.1	15.0	9.8	12.8	
	3.7	9.5	13.2	13.9	10.2	11.5	6 weeks
	3.2	7.7	10.9	12.6	8.3	12.5	5 years
Mrs. A. P.	7.0	9.3	16.3	16.0	8.1	12.2	
	5.5	9.5	15.0	16.2	7.5	12.1	10 days
	5.3	8.3	13.6	13.5	10.3	12.5	3 months
	4.3	9.5	13.8	13.1	9.0	12.4	5 months
Mrs. E. G.	4.4	11.2	15.6	15.3	10.6	13.2	
	4.4	8.7	13.1	14.5	8.2	13.2	4 years
Mrs. R. W.	5.2	10.7	15.9	15.2	10.3	12.3	
	5.5	9.8	15.3	14.8	9.5	12.2	2 weeks
	4.3	9.3	13.6	14.8	9.5	12.1	5 months
Mrs. J. R.	5.9	9.4	15.3	14.2	10.5	12.9	
	4.5	9.5	14.0	12.5	8.6	13.1	3½ weeks
	4.8	8.3	13.1	12.8	5.7	13.0	4 months
	5.0	8.5	13.5	13.2	10.7	13.0	11 months
Mrs. E. Mc.	5.5	9.1	14.6	14.2	9.1	12.0	
	5.8	8.4	14.2	13.9	7.0	12.1	1 week
	4.6	7.9	12.5	11.8	7.0	12.2	3 weeks
	4.2	8.9	13.1	12.5	9.5	12.4	7 months
	4.5	8.5	13.0	12.0	9.6	12.4	9 months
	4.2	9.2	13.4	13.4	13.7	12.8	1½ years
Mrs. A. F.	4.7	7.6	12.3	13.1	10.5	12.0	
	3.8	6.8	10.6	11.8	9.3	10.4	1 year
	2.8	7.4	10.2	12.5	10.0	10.9	1½ years
Mrs. A. H.	6.3	8.2	14.5	14.5	10.7	11.3	
	5.0	7.5	12.5	13.0	9.7	10.8	1 year

*After the beginning of medication.

TABLE III—(*Continued*)

Initials	Right	Left	Trans. Diam.	Length	Base	Half Diam. Chest	Time Interval*
Mrs. A. Mc.	4.1	8.7	12.8	13.0	8.6	12.9	
	3.1	8.8	11.9	13.0	8.7	12.9	3 weeks
	3.2	8.3	11.5	14.0	10.2	12.7	4 months
	3.3	7.5	10.8	12.8	6.1	12.3	5 months
	3.5	7.6	11.1	12.0	8.2	12.6	1 year
Mrs. L. Mc.	4.7	8.3	13.0	13.6	8.8	11.0	
	4.0	7.1	11.1	12.0	9.0	10.8	1 year
Mrs. A. G.	4.3	8.3	12.6	13.1	8.6	11.2	
	3.0	7.9	10.9	12.1	8.0	11.5	1 month
	3.2	8.2	11.4	12.1	7.2	11.8	11 months
Miss C. Mc.	5.0	10.7	15.7	15.0	11.5	14.3	
	5.7	8.7	14.4	14.7	6.8	14.2	9 days
	4.2	9.8	14.0	15.0	7.6	14.1	3 weeks
Mrs. E. M.	4.0	9.5	13.5	14.0	8.5	12.5	
	3.8	8.3	12.1	13.5	7.2	11.5	15 months
	3.4	9.4	12.8	13.3	7.2	12.3	7 years
Mrs. D. M.	4.7	6.8	11.5	12.4	8.6	11.8	
	3.8	6.3	10.1	11.3	6.7	11.6	10 months
Mr. J. W.	4.8	8.6	13.4	13.5	10.8	14.4	
	3.5	8.7	12.2	12.1	5.9	14.8	5 years
Mrs. E. S.	4.0	10.5	14.5	14.5	9.0	13.3	
	3.5	10.2	13.7	13.7	5.5	14.3	2½ years
Mrs. M. F.	4.1	8.8	12.9	13.5	8.9	12.7	
	5.1	7.6	12.5	14.6	10.5	12.7	2 months
	4.4	7.7	12.1	13.2	9.7	12.4	10 months
Mrs. M. B.	3.7	8.7	12.4	14.0	10.0	12.5	
	3.7	8.0	11.7	12.7	6.9	12.6	4 years
Mrs. E. O.	3.7	9.2	12.9	13.7	9.3	11.9	
	4.1	8.4	12.5	11.0	8.5	12.6	3 weeks
	4.3	8.2	12.5	12.7	6.3	12.6	14 months
Miss A. P.	5.0	9.0	14.0	12.5	9.0	12.5	
	5.6	8.0	13.6	13.6	6.5	12.5	3 years
Mrs. M. Mc.	4.9	10.1	15.0	14.8	10.0	13.1	
	3.8	10.9	14.7	14.6	6.8	12.9	1½ years
Mrs. M. L.	5.3	9.3	14.6	15.2	8.5	12.7	
	3.8	10.5	14.3	15.0	8.7	12.5	3 years
Mrs. J. C.	3.2	10.1	13.3	14.3	9.3	12.8	
	2.8	10.6	13.4	13.8	5.2	13.3	3 years
Mrs. E. D.	4.1	9.9	14.0	14.2	9.9	14.0	
	5.1	9.0	14.1	14.8	5.3	14.7	5 years
Mr. J. G.	3.3	10.4	13.7	12.7	8.5	12.8	
	2.7	11.5	14.2	14.8	6.6	12.9	3 months
	3.0	11.1	14.1	15.3	7.1	13.2	4 years

*After the beginning of medication.

TABLE IV
CHANGE IN SIZE OF HEART AND IN BLOOD PRESSURE AFTER THYROID MEDICATION IN 30 PATIENTS WITH MYXEDEMA

Patient	Age	Basal Metab. Rate	Half Trans. Chest Diam.	Trans. Heart Diam. before Rx	Max. Heart Change after Rx	Time Interval for Change	Blood Pressure before Rx	Blood Pressure after Rx
Mrs. N. C.	46	–28	13.0	19.3	6.9	6 mo.	180/130	148/104
Mr. R. M.	45	–37	15.8	21.4	5.7	6 wk.	175/115	–
Mrs. B. S.	42	–34	13.2	16.5	5.4	2½ mo.	118/ 90	110/ 70
Mr. E. J.	77	–30	14.7	19.4	3.9	5 mo.	145/ 90	125/ 70
Mrs. J. P.	49	–36	11.5	14.6	3.4	2 wk.	180/120	125/ 75
Mrs. L. C.	53	–45	12.8	14.1	3.2	5 yr.	140/ 70	150/ 70
Mrs. A. P.	44	–40	12.2	16.3	2.7	3 mo.	138/116	160/104
Mrs. E. G.	48	–35	13.2	15.6	2.5	4 yr.	120/ 65	155/ 90
Mrs. R. W.	36	–38	12.3	15.9	2.3	5 mo.	160/110	146/ 84
Mrs. J. R.	43	–28	12.9	15.3	2.2	4 mo.	165/110	120/ 76
Mrs. E. Mc.	70	–29	12.0	14.6	2.1	3 wk.	180/100	180/ 90
Mrs. A. F.	42	–39	12.0	12.3	2.1	1½ yr.	115/ 80	–
Mrs. A. H.	51	–30	11.3	14.5	2.0	1 yr.	148/100	154/ 94
Mrs. A. Mc.	47	–17	12.9	12.8	2.0	5 mo.	140/100	126/ 80
Mrs. L. Mc.	33	–30	11.0	13.0	1.9	1 yr.	125/ 80	115/ 75
Mrs. A. G.	45	–43	11.7	12.6	1.7	1 mo.	125/ 80	126/ 80
Miss C. Mc.	50	–29	14.3	15.7	1.7	3 wk.	130/ 90	–
Mrs. E. M.	41	–24	12.5	13.5	1.4	15 mo.	130/ 70	110/ 65
Mrs. M. D.	49	–31	11.8	11.5	1.4	10 mo.	142/ 76	120/ 78
Mr. J. W.	63	–32	14.4	13.4	1.2	5 yr.	160/ 75	120/ 70
Mrs. E. S.	43	–35	13.3	14.5	0.8	2½ yr.	110/ 85	138/ 80
Mrs. M. F.	42	–19	12.8	12.9	0.8	10 mo.	128/ 86	134/ 82
Mrs. M. B.	32	–45	12.5	12.4	0.7	4 yr.	112/ 65	110/ 70
Mrs. E. O.	70	–20	11.9	12.9	0.4	14 mo.	190/130	154/110
Miss A. P.	56	–34	12.5	14.0	0.4	3 yr.	160/120	178/106
Mrs. M. Mc.	55	–31	13.1	15.0	0.3	1½ yr.	165/115	148/ 90
Mrs. M. L.	49	–16	12.3	14.6	0.3	3 yr.	140/100	154/102
Mrs. J. C.	56	–31	12.8	13.3	–0.1	3 yr.	150/ 90	210/110
Mrs. E. D.	42	–35	14.0	14.0	–0.1	5 yr.	120/ 80	100/ 68
Mr. J. G.	53	–25	12.8	13.7	–0.4	4 yr.	130/ 90	128/ 76

Considering any heart above normal size where the transverse cardiac diameter is greater than half the internal diameter of the chest, then we find that 25 of the 30 patients had enlarged hearts, as follows:

Transverse cardiac diameter minus one-half internal chest diameter	No. of cases
cm.	
0 – 1.0	5
1.0 – 1.9	7
2.0 – 2.9	4
3.0 – 3.9	5
4.0 – 4.9	2
5.0 – 5.9	1
6.0 +	1

In the remaining five cases the transverse cardiac diameter was either equal to or less than half the internal chest diameter.

Of the 30 cases, 20 showed a maximum decrease in transverse diameter of the heart after treatment of more than one centimeter and seven of less than a centimeter, distributed as follows:

Decrease in transverse cardiac diameter	No. of cases
cm.	
0.1 – 0.9	7
1.0 – 1.9	6
2.0 – 2.9	8
3.0 – 3.9	3
4.0 – 4.9	0
5.0 – 5.9	2
6.0 – 6.9	1

The remaining three cases showed increases of 0.1 to 0.4 cm. The age of the patient bore no relation to the change in the heart size under therapy. As for sex, there were only four males in the series. The presence of hypertension did not prevent the heart from shrinking. In fact, nine of the 20 patients who showed changes in the transverse cardiac diameter of more than a centimeter had some degree of hypertension before treatment. However, in these cases the repeat teleoroentgenograms were obtained usually less than six months after the beginning of treatment so that the factor of hypertrophy due to long-standing hypertension did not obscure the picture. Moreover, the hypertension disappeared in five cases. There is a close relationship between the degree of cardiac enlargement before treatment and the amount of shrinkage in the heart under treatment. The greatest changes in the size of the heart occurred in the large hearts. Expressed mathematically, the coefficient of correlation between the degree of cardiac enlargement and the degree of cardiac shrinkage is $+ 0.70 \pm 0.067$ for all the cases, and $+ 0.83 \pm 0.050$ for the 20 cases which decreased more than one centimeter. Both figures are highly significant statistically. The tendency in general was for the heart to approach normal size under therapy. In the few cases that this was not fulfilled, usually some degree of hypertension persisted.

The decrease in size of the heart in myxedema under thyroid medication is a slow and progressive procedure, as indicated in table 3. Twelve patients had serial teleoroentgenograms during the first year of treatment. Ten of these showed progressive shrinkage in size of the heart, reaching a maximum in three weeks to ten months after the beginning of treatment. Two cases reached their maximum in three weeks, six in three to five months, one in six months and one in ten months. The last had no examination in the interval between two months and ten months after treatment, so that the maximum change might well have occurred before ten months.

As indicated in table 3 the changes in the heart occurred in all diameters. However, measurements of the length and base of the heart are difficult to make and are subject to greater errors than the transverse cardiac diameter. Consequently the latter is used in judging the degree of cardiac shrinkage. As a matter of fact, the actual shrinkage in volume of the heart was greater in some instances than the decrease in transverse diameter indicated. Assuming that the surface area of the heart in the teleoroentgenogram is a more accurate measure of the volume of the heart than the transverse cardiac diameter, we measured the surface area of the heart of the first two cases (N. C. and R. M.) before and after treatment. In the first case (figure 1) the maximum change in surface area was from 161.6 sq. cm. to 77.6 sq. cm., a decrease of 52 per cent. The decrease in transverse cardiac diameter was 36 per cent. In the second case (figure 2) the maximum change in surface area was from 190.8 sq. cm. to 137.4 sq. cm., a decrease of 28 per cent. The transverse diameter decreased 26.6 per cent.

As mentioned above, the transverse

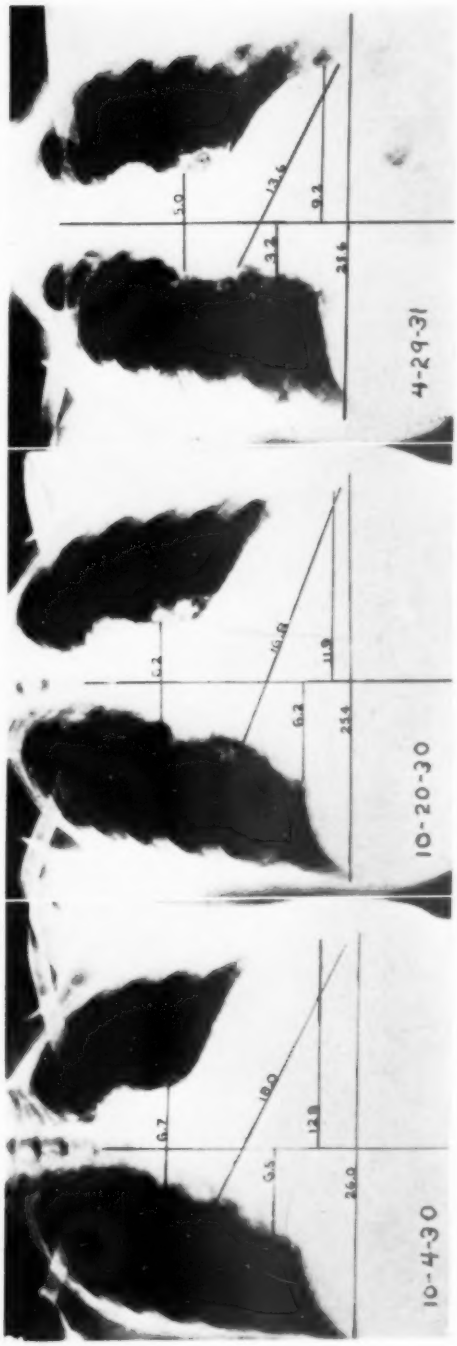

FIG. 1. Changes in the teleroentgenogram of patient (N. C.), at intervals of two weeks and six months after thyroid medication. The level of basal metabolism was minus 28 per cent; two weeks later it was minus 4 per cent; and six months later it was minus 3 per cent.

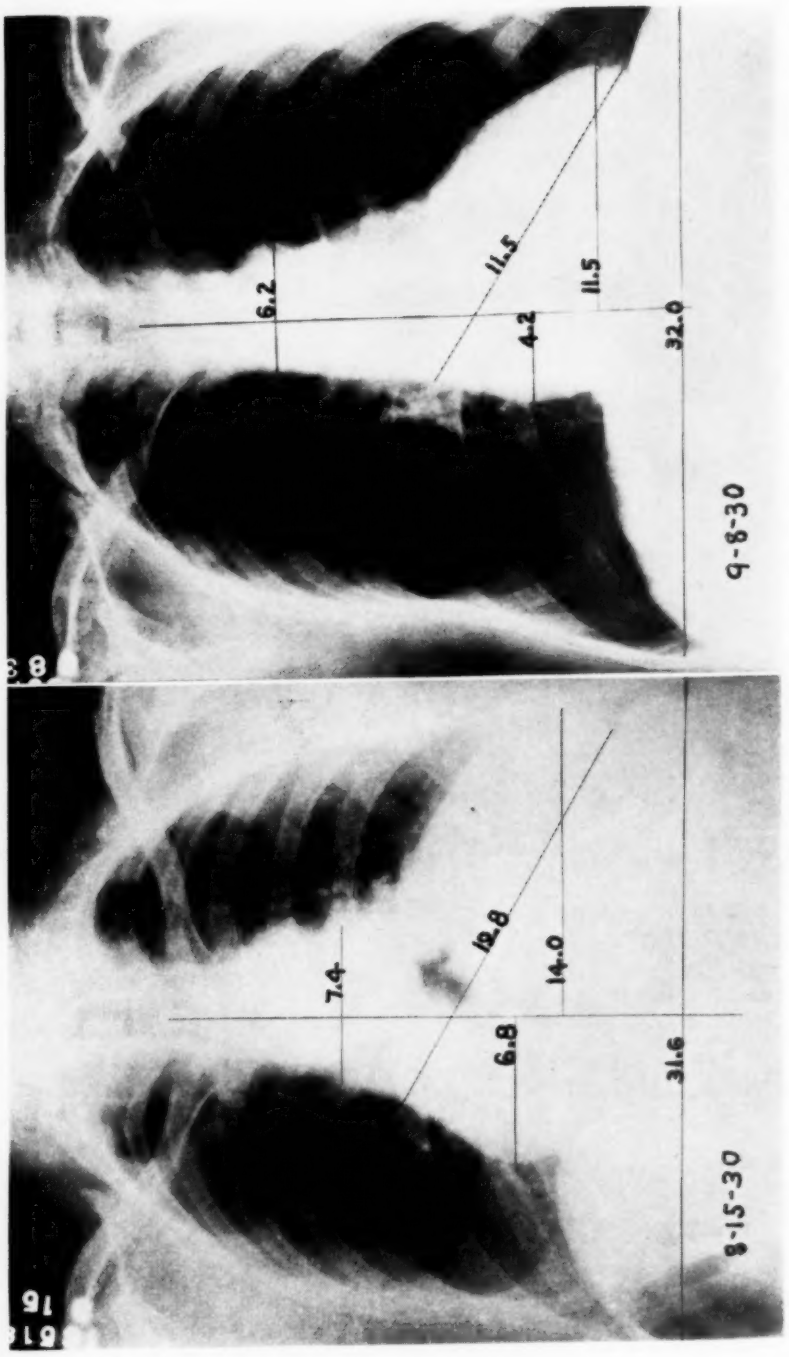

FIG. 2. Changes in the teleoroentgenogram of patient (R. M.), six weeks after thyroid medication. The level of basal metabolism was minus 37 per cent; and six weeks later it was plus 5 per cent.

diameter in ten cases decreased less than one centimeter or actually increased slightly under medication. The failure of these cases to show changes in the size of the heart may be explained for the most part by two factors. In the first place five of the patients (E. O., A. P., M. Mc., M. L., and J. C.) had persistent hypertension. Four of these had the first reëxamination of the heart one and one-half to three years after the beginning of treatment, and the fifth had the first reëxamination at three weeks and the second reëxamination at fourteen months. In these five cases, true hypertrophy might have been present at the beginning; or, if shrinkage of the heart had actually taken place, the cardiac hypertrophy due to hypertension during the long intervals between examinations might have masked it. The latter course of events was observed in one case (E. Mc.). This patient had a hypertension of 180 mm. of Hg systolic and 90-100 mm. diastolic. The transverse cardiac diameter was reduced from 14.6 cm. to 12.5 cm. in three weeks of treatment. At the end of nine months the transverse diameter was 13.0 cm. and at a year and one-half it was 13.4 cm.

The second explanation for the failure of this group of cases to show cardiac shrinkage is based on the above finding that the amount of shrinkage of the heart is proportional to the degree of cardiac enlargement. Consequently patients with normal hearts are not to be expected to show much change. Three (M. F., M. B., and E. D.) of the five remaining cases of this group had normal-sized hearts at the beginning of treatment. The fourth case (E. S.) had a normal-sized heart after the slight reduction in size had taken place.

It may be said in passing that the more carefully one follows patients with myxedema the more often will one find cardiac changes under treatment. Thus, of the 15 patients followed from the beginning of treatment, with this matter in mind, nine showed a decrease in transverse cardiac diameter of more than 2 cm., four of 1 to 2 cm., one of 0.8 cm., and the other of 0.4 cm.

Blood Pressure

Under thyroid medication the blood pressure underwent changes in 23 cases, either systolic, diastolic, or both, no change in four cases and was not followed in three. The systolic pressure dropped 10 mm. or more in 13 cases, rose 10 mm. or more in seven cases and underwent an insignificant change in seven. The diastolic pressure dropped 10 mm. or more in 14 cases, rose 10 mm. or more in two, and underwent an insignificant change in 11. The net result was a slight increase in pulse pressure. The latter rose 10 mm. or more in 13 cases, dropped 10 mm. or more in six, and underwent an insignificant change in eight. The patients with hypertension showed more marked changes than the remainder. Of the 14 patients with hypertension that were followed, five developed a normal blood pressure after treatment and six reached a lower level of hypertension, particularly in diastolic pressure. Only one patient with normal blood pressure before treatment developed hypertension after treatment.

Electrocardiograms

The matter of the electrocardiographic changes in myxedema appears to be on firm ground, but it was felt worth while to report the electrocardiograms in these patients both as adding to the evidence already at hand and for purposes of correlation with the roentgen-ray findings.

Electrocardiograms were obtained in 24 patients before and after treatment and are recorded in table 5. The most common abnormality in the electrocardiogram before treatment was flattening or inversion of the *T*-waves. This occurred 14 times in all leads, eight times in two leads and twice in one lead. The *T*-waves were abnormal in one or more leads in all 24 cases. The *T*-wave in Lead II was most commonly involved, i.e., in 23 cases; T_1 was involved in 22 cases and T_3 in 15 cases. In addition, nine electrocardiograms showed axis deviation, nine showed small complexes, one showed auricular premature beats, and one showed intraventricular block. The *P*-waves were low or flat in all but one case.

Under thyroid administration, 11 of the patients showed normal electrocardiograms at varying intervals after the beginning of treatment. Nine of these belong in the group whose hearts shrank more than one centimeter. In some instances the return to normal was delayed. In addition six lost their *T*-wave abnormalities and one lost his small complexes. Thus a total of 18 patients showed a disappearance of one or more of these abnormalities from their electrocardiograms. Four of the remaining six patients showed partial improvement of *T*-wave changes. The *P*-waves increased in size in 22 of the 24 cases. In all, 17 patients showed a complete disappearance of *T*-wave abnormalities

Table V

The Electrocardiogram in 24 Patients with Myxedema before and after Thyroid Medication*

Initials	Electrocardiogram before Treatment	Electrocardiogram after Treatment Time Interval in Parentheses
Mrs. B. S.	Low *T* all leads; low voltage.	Normal (6 wks.). Slightly slurred *Q-R-S*$_2$ and *Q-R-S*$_3$ (8 mos.).
Mr. E. J.	Left axis deviation; slightly inverted T_1; flat T_2 and T_3.	Partial A-V block; low *T*-waves; slight left axis deviation (2 wks.). Slightly inverted T_1; T_2 and T_3 + 3 mm.; slight left axis deviation (5 mos.).
Mrs. J. P.	Slightly inverted T_1; low T_2 and T_3; slurred *Q-R-S*.	Inverted T_1 and T_2; slight slurring *Q-R-S* (3 wks.).
Mrs. A. P.	Low voltage; low *T*-waves.	Low voltage; low *T*-waves; slight left axis deviation (2 wks.). Left axis deviation; normal T_1 and T_2; inverted T_3 (4 mos.).
Mrs. E. G.	Flat T_1; inverted T_2 and T_3; low voltage; slight left axis deviation.	S-A tachycardia; small complexes (4 yrs.).

*The *P*-waves are not recorded here. They were small in all but one case. Under medication they almost always increased in size.

TABLE V—(*Continued*)

Initials	Electrocardiogram before Treatment	Electrocardiogram after Treatment Time Interval in Parentheses
Mrs. R. W.	Diphasic T_3; flat T_3; tendency toward right axis deviation; small complexes.	Normal (9 mos.).
Mrs. J. R.	Left axis deviation; T_1 inverted; T_2 flat.	S-A tachycardia; left axis deviation; flat T_1 and T_2 (1 wk.). S-A tachycardia; left axis deviation; T_1 and T_3 + 3 mm.; T_2 normal (4 mos.).
Mrs. E. Mc.	Slight intra-ventricular block; inverted T_1; flat T_2.	Left axis deviation (10 mos.).
Mrs. A. F.	Flat T_1 and T_2.	Normal (3 wks.). Normal (1 yr.).
Mrs. A. Mc.	Flat T_1; inverted T_2; left axis deviation.	Normal (5 mos.).
Mrs. A. G.	Low T-waves all leads; low voltage.	Flat T-waves all leads; slight left axis deviation (1 wk.). Normal (1 yr.).
Miss C. Mc.	Inverted T_1; diphasic T_2; left axis deviation.	Low T-waves; left axis deviation (2 wks.). Low T-waves; left axis deviation (3 wks.).
Mrs. E. M.	Low T-waves all leads.	Low T-waves all leads; T_2 slightly higher (15 mos.). Normal (7 yrs.).
Mrs. M. D.	All T-waves flat.	Normal (1 yr.).
Mr. J. W.	Flat T_1; diphasic T_2; flat T_3; small complexes.	Normal (5 yrs.).
Mrs. L. C.	Inverted T-waves all leads; small complexes.	Normal (1 mo.).
Mrs. E. S.	Rather low voltage; low T_1 and T_2; flat T_3.	Normal T_1; Leads II and III not obtained (2½ yrs.).
Mrs. M. F.	Flat T_1; inverted T_2 and T_3.	Slight left axis deviation; low T-waves all leads (2 mos.). Low T_2 and T_3; slight left axis deviation (8 mos.).
Mrs. M. B.	Flat T_1; inverted T_2 and T_3; slight right axis deviation.	T-waves normal; slight right axis deviation (7 mos.).
Miss A. P.	Slight left axis deviation; inverted T_1.	Ventricular premature beats; left axis deviation; inverted T_1 (5 mos.). Slight slurring of Q-R-S; diphasic T_1 and T_2; flat T_3 (1 yr.). Marked left axis deviation; inverted T all leads (3 yrs.).
Mrs. M. L.	Slightly inverted T_1 and T_2; slight left axis deviation.	Low T_2 (2 wks.). Slight left axis deviation (3 yrs.).
Mrs. J. C.	Auricular premature beats; inverted T_1 and T_2.	Normal (3 yrs.)
Mrs. E. D.	Flat T-waves all leads; low voltage.	Inverted T_1; T_2 and T_3 + 6 mm.; slight left axis deviation; inverted Q-R-S_2 (5 yrs.).
Mr. J. G.	Flat T_2.	Moderate left axis deviation (5 yrs.).

whereas seven retained some abnormality. Small complexes were retained in only one of the nine cases. Six patients retained axis deviation and five additional patients developed this abnormality with treatment. However, six of these 11 patients had hypertension at the beginning of treatment, and six were in the group whose hearts decreased less than one centimeter. On the other hand the three patients who lost their axis deviation belonged in the group whose hearts decreased more than one centimeter. In general it would seem that the cases which showed the most marked shrinkage in the shadow of the heart were the ones whose electrocardiograms showed the most return to normal.

It has been suggested by Nobel, Rosenblüth and Samet[23] that resistance of the myxedema skin is the factor causing the abnormal electrocardiographic findings. By using needle electrodes to overcome skin resistance, they were able to change abnormal electrocardiograms to normal. The fallacy of this contention is that if the changes in the electrocardiogram are due to resistance of the skin, then all the complexes should be equally affected. On the contrary, in myxedema the *T*-waves show the most marked deviation from the normal. Dr. Paul D. White was good enough to test out the suggestion of Nobel et al by obtaining electrocardiograms with the usual electrodes and then with needle electrodes in two patients. The results are illustrated in figure 3. In one case the resistance was actually higher with needle electrodes than with the usual electrodes, in the other the resistance was about the same. With greater resistance a looser string was required so that overshooting and exaggerated complexes occurred but the character of these complexes was unchanged. Consequently electrocardiographic abnormalities are probably due to changes in the heart itself and not in the skin.

Other Findings

Fourteen patients at time of entry into the hospital showed no abnormality on auscultation. Four showed systolic murmurs, two had extra systoles and the remainder presented sounds of faint or poor quality. Cardiac enlargement as gauged by physical examination was found in nine cases. The size of the heart was under-measured on physical examination in 15 cases and in eight of these the undermeasurement was great enough to cause the diagnosis of normal-sized heart, whereas the roentgen-ray showed an enlarged heart.

Several of the cases in the literature presented signs of definite cardiac decompensation. Fahr[6,15] emphasizes cardiac failure as part of the picture of "myxedema heart". To be sure, many of our patients showed various degrees of peripheral edema but this may be accounted for on the basis of myxedema alone. Four patients showed evidence suggestive of cardiac failure, as follows: one (R. M.) showed crepitant râles at the lung bases and pitting edema over the extremities and sacrum; one (E. J.) showed a small amount of fluid in the right pleural cavity, palpable liver edge, and pitting edema of the extremities; and two (J. C. and E. O.) showed crepitant râles at the lung bases, palpable liver

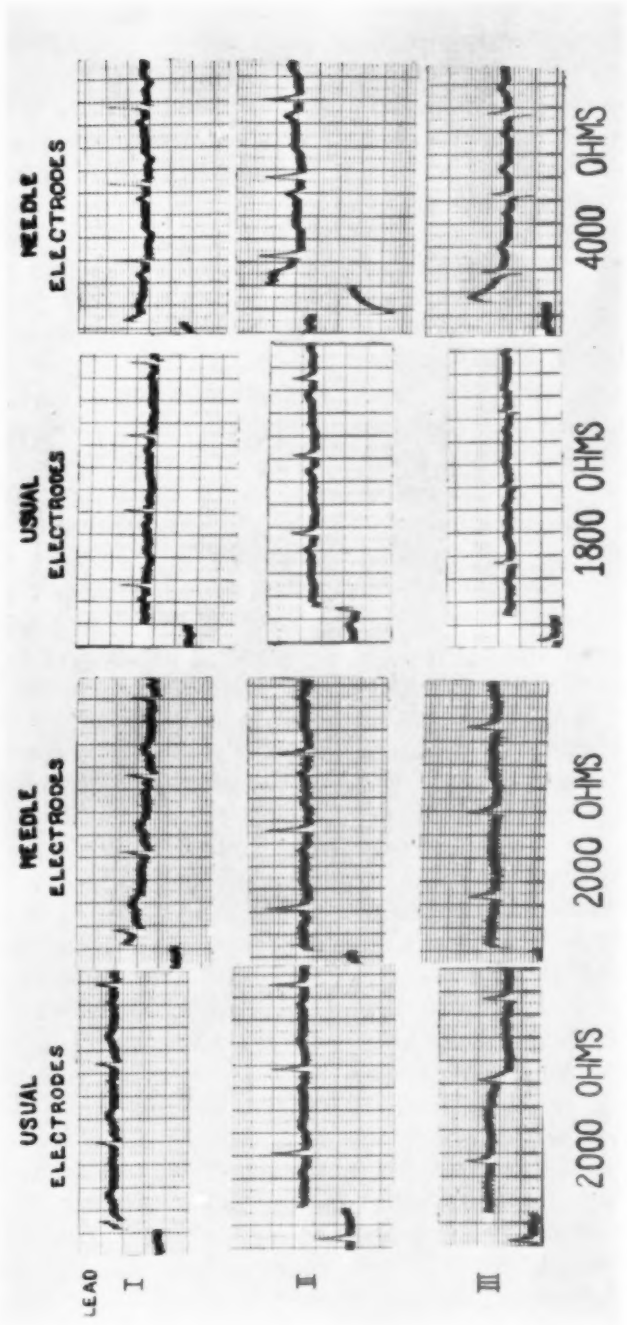

FIG. 3. Illustration of the effect of needle electrodes on the electrocardiogram. In one case the skin resistance was the same with needle electrodes as with the usual electrodes; and in the other the skin resistance was greater with needle electrodes than with the usual electrodes.

edge, and pitting edema. The evidence for cardiac failure was not conclusive in any of these. All the signs disappeared on rest and thyroid medication. The blood pressure was moderately elevated in each of these cases, and the peripheral vessels sclerosed in three. The patient presenting the most evidence of congestive failure (R. M.) died suddenly seven months after leaving the hospital, cause undetermined.

Discussion

One gathers the impression from a study of the literature that the cases reported by Zondek, Fahr, and others, in which roentgen-ray findings or photographs of the roentgenograms are given, are all thoroughly genuine. We believe that Fahr emphasizes the point of cardiac failure to a greater extent than his published findings warrant. In three of his cases,[15] dyspnea and edema could well be part of the general picture of myxedema rather than due to cardiac failure. Our impression of the report by Willius and Haines[8] is that their cases were not thoroughly worked up. The inclusion of patients with low metabolism but without myxedema may account for the finding of normal electrocardiograms in 54 per cent of their cases.

Moreover it is worth noting that Willius and Haines,[8] and Christian,[7] the two who are most emphatic in denying the existence of "myxedema heart" fail to mention roentgen-ray studies of the heart size. As indicated above, the heart in myxedema is frequently under-measured by physical examination before therapy is started. Consequently changes in the size of the heart might easily be missed, unless serial teleoroentgenograms are obtained.

Our studies lead us to believe that the heart in myxedema is usually enlarged and decreases in size when thyroid is administered and that the change in the size of the heart is of diagnostic importance. Cardiac failure due to myxedema is uncommon, and slight if present. It is practically always associated with hypertension and arteriosclerosis.

The nature of the decrease in heart size is difficult to understand, mainly because so little is known of the pathology of the heart in myxedema.* The best and most complete pathological description of myxedema cases is to be found in the report of the Clinical Society of London published in 1888.[25] The findings in 20 cases are reviewed. The left ventricle of the heart was hypertrophied in a third of the cases. In more than half there was atheroma of the arteries. Microscopic descriptions are given in only nine cases. Three of these showed evidence of interstitial myocarditis.

At the Massachusetts General Hospital we have been able to trace the records of five autopsies on myxedema patients. Three died as a result of complicating infections, one died of an unknown cause, and one died of hypertensive and arteriosclerotic heart disease before the myxedema could be treated. Four showed interstitial edema with more or less fibrosis of the heart muscle, and the fifth showed fibrosis only. Two of the patients had not

*The nature of the heart in myxedema is discussed by one of us (J. H. M.[24]) in a recent article.

received any thyroid medication. It seems likely that the edematous condition present in other tissues in myxedema is also present in the heart muscle. Therefore the changes in the heart should be regarded as part of the picture of myxedema and not as a separate entity.

Experimentally, the removal of thyroids in animals causes gross alterations in the cardiovascular system. Among others, Goldberg[26] showed that sheep and goats made cretinoid by removal of their thyroids, developed cardiac dilatation and a flabby myocardium.

On the basis of the above facts, one is justified in making the tentative assumption that administration of thyroid extract decreases the size of the heart in myxedema by causing the loss of interstitial edema and by increasing the muscle tonus.

It has been suggested that pericardial effusion may account for the size of the heart and that disappearance of fluid with thyroid medication may account for the apparent cardiac shrinkage. This is of interest in view of the finding of the London Committee[25]: "Anasarca to a slight degree was not uncommon, though in no instance was it excessive. On the other hand, passive effusions into serous cavities, sometimes to a considerable amount, were frequently noted." While they do not specifically report any case with pericardial effusion, their findings suggest that this condition may occur. Both of our autopsied patients who did not receive thyroid before death had fluid in the pericardial sac — one a small amount (150 c.c.) and the other a large amount (1+ liters). The latter patient possessed the complicating factors of hypertension and arteriosclerosis. Moreover, Goldberg[26] found pericardial fluid in seven of 18 sheep with experimental myxedema. In most cases, however, neither the clinical findings nor the roentgen-ray picture of the heart are consistent with significant amounts of pericardial fluid.

Conclusions

The heart is generally enlarged in myxedema. After thyroid medication, the size of the heart, in most cases, undergoes a progressive shrinkage, which reaches its maximum as a rule in three to six months. This decrease is of diagnostic value. The amount of reduction in the size of the heart is proportional to the degree of cardiac enlargement. The failure of some patients to show cardiac change after thyroid medication may be explained on the basis either of long standing hypertension or of the fact that the heart is not enlarged before treatment.

The blood pressure in myxedema is often elevated above normal. With treatment there is a tendency for both systolic and diastolic pressures to fall, particularly the latter. The net result is a slight increase in pulse pressure. The most marked reductions in blood pressure occur in patients with hypertension.

The electrocardiogram in myxedema is always abnormal. The most common abnormality is a flattening or inversion of the *T*-waves, particularly in Lead II. In addition, abnormal axis deviation and small *P* and *Q-R-S* complexes are common. On thyroid treatment, many of the abnormalities disappear wholly or in part. The greatest

return to normal occurs in those patients with the most marked shrinkage in the size of the heart. The abnormalities in the electrocardiograms are probably not due to increased skin resistance but to changes in the conduction system of the myocardium.

"Myxedema heart" in the sense of cardiac enlargement which undergoes shrinkage on thyroid medication is common; in the sense of Zondek and Fahr, i.e., cardiac enlargement in association with congestive failure, it is rare. The heart changes are to be regarded as part of the picture of myxedema, not as a separate cardiac entity. The patients with findings suggestive of cardiac failure usually have hypertension and arteriosclerosis.

The change in the heart with thyroid treatment is probably due to increased muscle tonus and loss of interstitial edema. In an occasional case the loss of pericardial fluid may account for this change.

We are indebted to Dr. P. D. White for his valuable assistance during the course of this work.

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Heredity in Diabetes*

By William Allan, M.D., *Charlotte, North Carolina*

THE impression prevails that diabetes mellitus is in some degree hereditary. In discussing this matter Joslin[1] cites the frequency of a history of diabetes in grandparents, parents, uncles, aunts, and children as the group of relatives indicating hereditary tendencies, and the frequency of diabetes in siblings and cousins as indicating familial occurrence of diabetes. In two series of diabetic persons numbering 2,800 and 2,646 he finds the frequency of a history of diabetes in the "hereditary group" to be 15 per cent and 17 per cent respectively. His figures for the familial occurrence of diabetes in his two series are 7 per cent and 12 per cent respectively, while I secured a history of diabetes in sibs and cousins in 25 per cent of 143 diabetics. If his patients belonged to separate families the number of "hereditary group" relatives would be 108, 920 giving a diabetic incidence of approximately .8 per cent, which as he points out is not far from the incidence of diabetes in the general population at any time.

This method of evaluating the hereditary factor in diabetes seems unlikely to lead to anything definite. Would it not be better to take the incidence of diabetes in the general population, determine the expected incidence of diabetes in parents, siblings, and children[2] and compare these figures with our actual findings? Joslin (page 131) estimates the incidence of declared and potential diabetes at about 1.4 per cent. If diabetes were inherited as a dominant unit character, it should appear in one or both parents in 100 per cent of instances: the actual finding of 10 per cent to 15 per cent of parental diabetes is so far from the expected incidence that it seems useless to consider further the inheritance of diabetes as a dominant character.

If diabetes were a unit recessive trait,
Let D = gene for normal or non-diabetic condition
d = gene for diabetes
p = frequency of D
q = frequency of d
Then $p + q = 1$
The possible combinations of these factors are expressed by the equation $(p + q)^2 = 1$, and the chance association of genes is shown in figure 1.

	D (p)	d (q)
D (p)	DD (p^2)	Dd (pq)
d (q)	Dd (pq)	dd (q^2)

Fig. 1.

$p^2 + 2\,pq$ = non-diabetics
q^2 = diabetics
$q = \sqrt{\text{diabetics}}$

Substituting Joslin's figure for the incidence of diabetes, 1.4%

$q = \sqrt{.014} = .1185$
$p = 1 - q = .8815$

Substituting the values of p and q in the foregoing equations

p^2 = pure or homozygous non-diabetics = 77.7 (DD)
2pq = hybrid or heterozygous non-diabetics = 20.9 (Dd)
q^2 = diabetics = 1.4 (dd)

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Within the non-diabetic group are the following ratios:

Homozygous non-diabetics = 78.8%
Heterozygous non-diabetics = 21.2%

The incidence in the general population if diabetes were recessive is shown in figure 2.

	DD .777	Dd .209	dd .014
DD .777	1 .6037	2 .1624	3 .0109
Dd .209	4 .1624	5 .0437	6 .0029
dd .014	7 .0109	8 .0029	9 .0002

1. DD×DD=DD DD DD DD=60.37%
2. DD×Dd=DD DD Dd Dd=16.24
3. DD×dd = Dd Dd Dd Dd = 1.09
4. Dd×DD=DD DD Dd Dd=16.24
5. Dd×Dd=DD Dd Dd dd = 4.37
6. Dd×dd = Dd Dd dd dd = .29
7. dd ×DD=Dd Dd Dd Dd = 1.09
8. dd ×Dd = Dd Dd dd dd = .29
9. dd ×dd = dd dd dd dd = .02

100.00%

FIG. 2

If diabetes were a recessive unit character with an incidence of 1.4%:

(1) One or both parents should have it in 22% of instances.

One-half of mating 6 = Dd×dd = .145
One-half of mating 8 = dd ×Dd = .145
Mating 9 = dd ×dd = .02

Total incidence 1.4).310(.22

In 143 cases I secured a history of diabetes in one parent in 17 instances, or 12%.

(2) Both parents should have it in 1.4%

Mating 9 = .02

$\frac{\text{Mating 9} = .02}{\text{Total Inc. } 1.4} = 1.4\%$

Only twice have I encountered diabetes in both parents, but Joslin reports diabetes in both parents 42 times in 4675 cases, giving an incidence of .9%.

(3) One parent should have it in 20.7%
One-half mating 6 = Dd×dd = .145
One-half mating 8 = dd×Dd = .145

Total incidence 1.4).290(.207

My figures show 12%.

(4) Neither parent should have it in 78%

One-fourth mating 5=Dd×Dd=¼×4.37

$\frac{\text{One-fourth mating } 5=\text{Dd}\times\text{Dd}=\frac{1}{4}\times 4.37}{1.4} = .78$

In 88% of 143 cases I failed to obtain a diabetic history in either parent.

(5) If both parents have diabetes, then 100% of the children should have it. I have encountered diabetes in both husband and wife only twice; in one instance there were no children and in the other the number of diabetic children was unknown.

(6) If one parent has diabetes, 10.6% of the children should have it.

	DD .788	Dd .212					Dd	dd
dd	1	2	1 = Dd	Dd	Dd	Dd = 78.8%	78.8%	
1.00	.788	.212	2 = Dd	Dd	dd	dd = 21.2	10.6%	10.6%

I have not been able to find in the literature any figures on the percentage of children with diabetes when either one or both parents have it.

(7) If neither parent has diabetes, 1.125% of the children should have it.

	DD .788	Dd .212				
DD .788	1 .621	2 .1670	1 = DD	DD	DD	DD = 62.10
			2 = DD	DD	Dd	Dd = 16.70
			3 = DD	DD	Dd	Dd = 16.70
Dd .212	3 .1670	4 .045	4 = DD	Dd	Dd	dd = 4.50

DD	Dd	dd
62.10%		
8.35	8.35%	
8.35	8.35	
1.125	2.25	1.125%

(8) If diabetes is recessive with an incidence of 1.4%, then 31.3% of the sibs of diabetics should have it.

One-fourth	mating 5 = 1.09	: diabetic sibs	25% = .273
One-half	mating 6 = .145	: diabetic sibs	50% = .0725
One-half	mating 8 = .145	: diabetic sibs	50% = .0725
	Mating 9 = .02	: diabetic sibs	100% = .02
	1.4	Total inc.	1.4).4380(31.29

I have only 24 separate families in which there was a history of diabetes in the sibs. These 24 diabetics had 36 sibs with diabetes, but the total number of sibs was not recorded. Taking 4.3 per cent as the average number of sibs there should thus be a total of 103 sibs in these 24 families, 36 or 35 per cent of whom have diabetes. As an actual fact in 15 of these families there were 101 children, that is, 86 sibs among whom there were 25 diabetic sibs which gives 29 per cent. But 143 diabetic patients would theoretically have 615 sibs and, as I secured a history of diabetes in only 36, this is only about 6 per cent.

(9) If diabetes is recessive with an incidence of 1.4%, then .98% of the sibs of non-diabetics should have it.

Three-fourths	mating 5 = 3.28	with diabetic sibs 25% = .82
One-half	mating 6 = .145	with diabetic sibs 50% = .0725
One-half	mating 8 = .145	with diabetic sibs 50% = .0725
	Total incidence	98.6) .9650(.98

I have no data on the frequency of diabetes in the sibs of non-diabetics.

Summary

The data available at present are much too meager to warrant drawing any conclusions, but it seems possible that diabetes may be transmitted as a recessive unit character.

Discussion

Since these notes were written about eighteen months ago, Wright[3] has published an interesting discussion of "hereditary and familial diabetes mellitus", illustrated by nine charts of diabetic family pedigrees. He considers diabetes to be the product of two factors, an hereditary factor plus an acquired factor such as infection or obesity. Although none of his charts shows diabetes in more than two successive generations, he apparently follows Cammidge in believing that diabetes is sometimes a recessive trait (when severe in the young) and sometimes a dominant trait (when mild in the old).

Howard and Cammidge[4] found that high fasting blood sugar in mice is transmitted as a unit recessive Mendelian trait, and Cammidge[5] states "since the abnormality of carbohydrate metabolism giving rise to a high fasting blood sugar in animals is undoubtedly a recessive character, it is not unlikely that similar defects in the chemistry of the body of human beings may be transmitted in the same way, and that some forms at least of hyperglycemia and glycosuria, or the conditions predisposing to their development, may consequently run in families like a high fasting blood sugar in mice."

Cammidge discounts statistical studies and undertakes to illustrate the inheritance of human diabetes by family pedigrees of two or three generations, with half a dozen members in each generation, and promptly encounters the dilemma of pedigrees that correspond to both dominant and recessive traits, or to neither. In addition since his cases are not controlled by blood sugar reports, alimentary glycosuria, which is hereditary, may be a confusing element. Hence it seems wiser to stick to statistical studies, unless much more extensive family surveys can be made.

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Undulant Fever: A Fatal Case*†

By R. C. Rothenberg, M.D., *Cincinnati, Ohio*

THERE have recently been numerous clinical publications on undulant fever. Kern,[1] in 1928, summarized the 36 abortus strain cases previously cited in the American literature and added two more. Simpson and Fraizer[2] in 1929, and Simpson[3] in 1930, recorded the findings in a group of cases near Dayton, Ohio. In the latter year Giordano and Sensenich[4] reported a clinical analysis of 35 cases in Indiana. In the same year (1930) Hardy's[5] extensive study in Iowa mentioned ten fatal cases, with gross and microscopic autopsy findings in two.

While the mortality rate has been placed by Hardy at 3 per cent, there are relatively infrequent references in the literature to fatal instances of the disease. The following case is reported because of the unusual opportunity to study the patient for a long time, and to follow him to the necropsy table.

Case Report

W.J., aged 57, a farmer, who had lived in Michigan all his life, entered the University Hospital December 2, 1930, in the fifth month of an illness that had begun suddenly on July 6, 1930. The onset had been marked by cough, expectoration of large quantities of tenacious sputum, chills and fever, drenching night-sweats, soon followed by generalized arthralgia, and by moderate dyspnea accompanying his usual activities. On July 15 a diagnosis of undulant fever had been made as a result of agglutination studies in a nearby laboratory (titer: Br. abortus 1:100). In the same laboratory one month later the titer was again significantly positive (Br. abortus 1:250).

Treatment with "convalescent serum" had produced a remission of symptoms for two weeks soon after the onset; then all symptoms had recurred and two more treatments with serum had afforded no improvement. In August, a series of rectal instillations of a "blue dye" had been of no avail. All symptoms had persisted until the time of admission to the hospital, although the arthralgia had become much less severe and the dyspnea more pronounced. The patient had been confined to bed since the exacerbation, about August 1, a period of four months. For three weeks before entrance there had been gradual swelling of the abdomen and slight edema of the ankles, accompanied by oliguria. The temperature had risen to 101° or 101.5°every afternoon since the onset.

The patient had been married for thirty-two years; there were no offspring. The remainder of the history was irrelevant. There had been no other illness with the exception of mild scarlatina in childhood. The man had been actively engaged in tending his farm, assisting in strenuous manual tasks until the sudden onset of this disease.

A possible source of infection existed in the patient's herd of cattle, three cows recently purchased having aborted. The patient stated that he drank raw milk only in hot coffee. No similar infection had occurred

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†From the Department of Internal Medicine, University of Michigan, Ann Arbor, Mich.

in any member of the patient's household. Agglutination of his wife's blood was negative. Subsequent bacteriological examination of milk samples in our laboratory failed to demonstrate brucella organisms.

The essential features of the physical examination were evidence of general weakness, moderate loss of flesh, ascites, and bilateral pretibial edema. The lungs showed only slight congestion at the right base. The heart was normal in position, size, and action; there was electrocardiographic evidence of small complexes and slight left ventricular preponderence. The palpable peripheral arteries were moderately sclerosed. The blood pressure was 114/72. A smooth liver edge could be felt 3.5 centimeters below the right costal margin. The spleen extended one finger's breadth below the ribs on the left.

The urine showed a trace of albumin at a few examinations. There were usually a few white blood cells in the sediment and occasionally a red corpuscle. A Lashmet-Newburgh[6] concentration test for kidney function gave a maximum value of 1.022, a reading slightly below normal for the method employed. The red blood cell count varied from 4,100,000 to 5,300,000, and the hemoglobin from 75 to 87 per cent on the Sahli scale. A leukopenia was a rather constant feature. The white cells averaged 4200 on ten examinations, with a range between 3200 and 7900. A terminal rise to 17,000 occurred. The average polymorphonuclear percentage was 53, and there was a slight relative lymphocytosis, with an average of 42 per cent. The character of cells and platelets was normal at all times.

The stool was normal. The sputum was clear, of mucoid consistency, and contained no organisms. Two examinations of the ascitic fluid showed it to be cider-colored, clear, neutral to litmus, with specific gravity of 1.007 to 1.010, and containing an average of 7000 cells per cubic millimeter, chiefly lymphocytes. There were also mesothelial cells, but no neoplastic cells.

The Kahn test on the blood serum was negative. Blood non-protein nitrogen and blood bilirubin values the day after admission to the hospital were respectively 34.2 milligrams per cent, and 6 milligrams per 1000 c.c. (indirect reaction).

Four blood cultures were negative. Cultures of the urine and ascitic fluid, and of the stool by the technic of Amoss and Poston[7] gave no growth.

Agglutination values were as indicated in the table. The titer remained at a significantly high level throughout the period of observation, being always highest for the melitensis strain. The variation between melitensis agglutination and that for abortus, while usually a difference of only one dilution, was occasionally more marked, a finding of interest which is at variance with the reported studies of some authors.* The absence of any cross-agglutination with members of the typhoid group is worthy of mention. The presence of agglutinins for brucella organisms in the ascitic fluid confirms the previously recognized fact that secretions from the serous cavities can agglutinate various bacteria in the presence of infection with those bacteria.

The clinical course of the disease during 133 days in the hospital is shown on the chart. The temperature was of intermittent character, with several short apyrexial periods. These give to the curve an irregularly undulant appearance, somewhat like some of the temperature types illustrated in the reports of the Mediterranean Fever Commission in 1905.[8] Similar findings have been recorded by Craig,[9] Giordano,[4] and other writers in their more chronic cases.

The pulse and respiration showed ranges generally proportional to the temperature, although at times the heart rate was relatively slow.

Loss of weight was progressive, associated with increasing weakness. The cough and sputum disappeared soon after admission and under maintenance doses of digitalis there was no longer dyspnea at bed rest. The use of a neutral diet with ammonium chloride

*Additional unpublished data are at hand which show a similar variation in undulant fever cases. In these, agglutination for *Brucella suis* was also studied, and this titer likewise showed no constancy in value nor in relationship to the others.

and, in addition, the intravenous administration of Salyrgan failed to control the accumulation of ascites, necessitating several paracenteses, as illustrated.

Two courses of brucella vaccine were given according to the method recommended by Simpson.[3,10] The second saline suspension contained twice as many brucella organisms (abortus and melitensis strains) as the first. Although no specific *intradermal* test was tried with these preparations, which were given subcutaneously, after the first injection with the stronger solution there appeared a localized red area which became indurated, in a manner entirely comparable to the reaction obtained with saline intradermal brucella antigens.

No appreciable result was obtained by either course of vaccine therapy. The clinical progression was steadily downward. Erysipelas of the face developed about a week before death, but cleared completely under treatment with continuous magnesium sulfate dressings. There was evidence of terminal pneumonia in both lower lobes. Exitus occurred on April 13, 1931, the 283rd day of disease.

The significant autopsy findings were as follows: 3400 c.c. of ascitic fluid were recovered and 200 c.c. of effusion were present in each pleural cavity. The pericardial sac was under slightly increased tension due to the presence of 150 c.c. of fluid. The heart was flabby, with a moderate excess of overlying fat. Microscopically, it showed brown atrophy, and slight endocardial sclerosis with fibrosis extending into the myocardium. Bilateral basal confluent lobular pneumonia was evident as were also chronic passive congestion and chronic edema of the lungs. The liver was atrophic, with moderately sharp and pointed edges. The capsule was of normal thickness, and showed numerous small grayish nodules over its surface. The organ cut with increased resistance. There was marked increase of connective tissue, chiefly perilobular in distribution. Occasional yellowish-gray areas of lipoid deposit and moderate congestion were seen. Under the microscope, chronic passive congestion, patchy fatty infiltration, and irregularly distributed chronic parenchymatous hepatitis of the type of atrophic cirrhosis were distinguished. Chronic interstitial pancreatitis was noted. There was atrophy, passive congestion, and parenchymatous degeneration of all organs.

The spleen and testes were of prime interest, the former because of its important place in all references since the earliest writings about undulant fever, the latter particularly because of its association as a complication in the disease, orchitis being prominently mentioned by Simpson,[3] Hardy,[5] and others.

Grossly, there were diffusely scattered pin-

DATE	BLOOD				ASCITES			URINE		
	BR. ABORT.	BR. MELIT.	B. TULAR.	TYPH. GR.	BR. ABORT.	BR. MELIT.	TYPH. GR.	BR. ABORT.	BR. MELIT.	TYPH. GR.
12-2-30	1:320	1:640	—	NEG.						
12-4-30	1:640	1:1280	—	NEG.	1:80	1:160	NEG.			
12-5-30	1:320	1:640	—	NEG.				NEG.	NEG.	NEG.
12-14-30										
12-15-30					1:40	1:80	NEG.			
12-26-30	1:160	1:320	—	NEG.						
1-6-31	1:160	1:160	NEG.	—						
1-19-31					1:80	1:160	—			
3-10-31	1:80	1:320	—	—						
3-13-31					1:20	1:80	—			
3-30-31					1:40	1:80	—			
4-7-31	1:160	1:320	—	—						
4-14-31 (POST-MORTEM)	1:80	1:320	—	—	1:40	1:160	—			

FIG. 1. Agglutinin values. Typhoid Group includes B. Typhosus, B. Paratyphosus A., and B. Paratyphosus B.

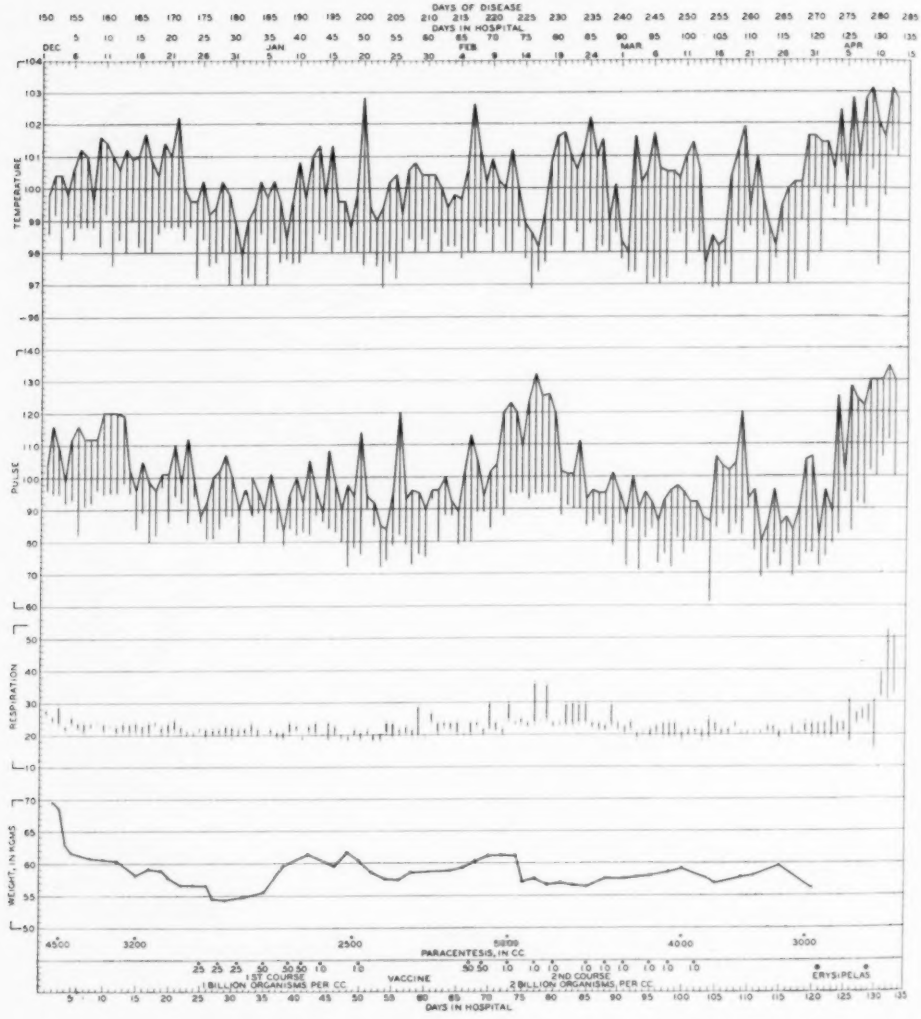

FIG. 2. Course of the disease during hospitalization. Each vertical column represents one day, with range from minimum to maximum for temperature, pulse, and respiration.

head sized, reddish, translucent nodules on the splenic surface, somewhat resembling tubercles. These proved microscopically to be localized areas of perisplenitis with hyaline change. The spleen was slightly enlarged with rounded edges. The capsule was thickened. There was lymphoid hyperplasia throughout. The sinuses were dilated and contained numerous macrophages in which red blood cells and blood pigment were engulfed. A few multinucleate giant cells were also present in the sinuses.

The testes revealed complete aspermatogenesis, with evidence of active interstitial orchitis, and scattered areas of fibroid atrophy. Vacuolar degeneration of the epithelium was noted. The prostate and seminal vesicles were normal.

DISCUSSION

Whether these pathological changes may be considered specific of undulant fever is open to question. The patient

died because of arteriosclerotic heart disease and cirrhosis of the liver. It is unlikely, however, that without the concomitant undulant fever impaired function of these organs would have been manifested when it was, or that death would have ensued when it did. On the other hand, it is entirely possible that without the hepatic damage and cardiac weakness the undulant fever would have run a shorter and more favorable course.

The precedent history of sterility does not permit an opinion that the aspermatogenesis was due to undulant fever. The active orchitis, however, can be more justifiably related to this disease.

It is interesting that both of Hardy's[5] cases showed hepatic damage and cardiac involvement at autopsy after a rather chronic course of illness.

In the present instance it seems at least highly suggestive, in view of the previous vigorous health, that the visceral damage resulted from the prolonged brucella infection.

Summary

A prolonged fatal case of undulant fever is presented and discussed with reference to its clinical, laboratory, and pathological considerations.

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Subacute Yellow Atrophy of the Liver Following Ingestion of Cinchophen and Allied Compounds*†

By Walter K. Grigg, M.D., and Victor C. Jacobsen, M.D.,
Albany, New York

CINCHOPHEN was first introduced to therapeutics in 1908 by Nicolaier and Dohrn for the treatment of gout. Since then its use has been extended to arthritis in general and as an analgesic. Various closely allied chemical compounds and derivatives have been brought out from time to time until now there are many similar drugs on the market, and with the multiplicity of trade names it is doubtful whether persons using or prescribing them are fully acquainted with the toxicity which they possess. Rabinowitz[1] has listed twenty in this group of remedies, and there are probably others.

The toxicity of these preparations has obtained considerable notoriety in the past few years. The occurrence of fatalities and of less serious complications has been so frequent that recently it has drawn editorial comment in the *Journal of the American Medical Association*.[2] The data of carefully studied cases of such poisoning should be published in order to stimulate the development of proper safeguards.

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†From the Departments of Medicine and Pathology of Albany Medical College and Albany Hospital.

Case Report

The case we wish to describe is that of a feeble white woman, aged 68 years. For many years she had been troubled with arthritis, involving especially the shoulders and hands. She had used many different remedies, the names of which could not be learned. It was noted by the family that for the two years prior to death, she had been growing weaker, was unable to accomplish her housework in a satisfactory manner, and had nervous manifestations, such as incoördinated twitchings of various muscle groups. She had lost from ten to fifteen pounds in the past year, although her appetite was good and she ate well without complaining of gastrointestinal symptoms.

During the three months she had been under our observation her chief symptoms were extreme weakness, slight incoördination of muscular movements accompanied by twitching, insomnia, arthritis of shoulders and hands, and loss of weight. Examination of heart, lungs, and kidneys showed nothing abnormal.

She was given occasional doses of luminal (½ gr.) for nervousness and insomnia with good results. Occasionally she would take two or three teaspoonfuls of whiskey in warm milk at bedtime. For arthritis she was given cinchophen intermittently—averaging two tablets daily for a few days and then stopping for a few days. She took about 35 tablets (262.5 grains) in the last two months. She was also given at other times oxyl-iodide, about two capsules daily for a few days, the drug then being discon-

tinued for several days. Of this she took about 25 capsules (75 grains). It was learned that prior to coming under our observation she had used atophan for various periods, the amounts or rate not being known.

About two months previous to death she had two acute spells of chills and fever, lasting about one and a half days each, about two weeks apart. The temperature reached 101°-102°. The symptoms each time cleared up entirely on rest in bed for a day. Leukocyte counts were within normal limits on both occasions.

On March 31, jaundice was noted. About two days before this she had taken one capsule of oxyl-iodide, but this had caused nausea, and no more of the drug had been used. The jaundice rapidly became very intense. There was no apparent diminution in the intensity of the jaundice, either clinically or by observation of urine. The urine showed albumin, hyaline and finely granular casts, and an occasional red cell. Bile was present.

The jaundice continued for about four weeks, until death intervened. The stools were clay colored for the most part, although occasionally a small amount of bile coloration could be seen. About a week before death, toxic symptoms became more prominent. Her speech was somewhat thick, and she was quite drowsy, and finally two days before her death she lapsed into a semicomatose condition from which she would arouse only momentarily. The forcing of fluids was followed by edema of the legs, but this subsided somewhat when she was put on a Karrell diet. Toward the end there was marked tympanites, but ascites was not noted until about two days before death. Her temperature was normal throughout this later period. It is worthy of note that after the appearance of jaundice she had no subjective symptoms of arthritis.

Necropsy was performed one and a half hours post mortem.

Anatomical Diagnosis: Subacute yellow atrophy of the liver; jaundice; dilatation of the mesenteric veins; bronchopneumonia.

The *body* is fairly well developed and nourished, 61 inches long. There is slight edema of the ankles. The skin is markedly jaundiced and the sclerae are deep yellow. No teeth are present. There is a small pigmented mole at the right external canthus and numerous small pigmented moles on the chest and back. Varicosities of the veins of both legs are present.

The abdominal fat is deep yellow, 3 cms. thick. Throughout the body the tissues are markedly jaundiced.

Peritoneal Cavity: Contains about 400 c.c. of clear, bile-stained fluid. There are firm adhesions about the spleen, gall-bladder, and appendix. In the area of the gall-bladder and the under surface of the liver the tissues are very edematous.

Pericardial Cavity: Contains a normal amount of bile-stained fluid.

Heart: Normal in size. Pericardial fat is normal in amount but is deeply bile-stained. The coronary arteries are very slightly thickened and on section the myocardium presents numerous grey plaques and streaks. The endocardium is smooth and glistening throughout. The edges of the mitral valve are slightly thickened.

Lungs: The external surface of the right lung is mottled grey. The lower lobe is slightly more firm and deeper in color. There is a scar at the apex. On section there is congestion and edema of the lower lobe. The left lung resembles the right.

Spleen: Is light grey and presents several irregular, deeply pigmented areas. On section the cut surface is firm and deep red.

Gastrointestinal Tract: Normal except for a few small areas of injection in the mucosa.

Pancreas: Is normal but the tissues about the pancreas present marked edema and bile staining.

Liver: Is small, firm, and nodular. Weight 650 gms. The external surface is bile-stained and marked by numerous small nodules. It cuts with considerable resistance, and the cut surface is bile-stained, hard and fibrous and irregularly lobulated. In the upper posterior part of the right lobe is an area about 8 by 5 cms., smooth and practically normal. The middle of the left lobe on its anterior surface is also quite smooth and lies below the level of the nodular tissue. The veins of the falciform ligament are markedly dilated.

Gall-Bladder and Ducts: There is much

edema and bile staining in the tissues about the gall-bladder. The ducts are patent but there is a very little bile in the gall-bladder. The mucosa of the gall-bladder is grossly normal. No stones are found.

Kidneys: Right is of normal size. There are numerous small subcortical cysts. On section the cut surface is markedly bile-stained. The cortex averages 5 mms. and

Lungs: Scattered foci of acute pneumonitis.

Spleen: Normal.

Pancreas: Normal except for a rare focus of acute interstitial pancreatitis.

Adrenal: Normal.

Stomach: Normal.

Duodenum and Jejunum: Perivascular lymphoid cells and eosinophiles are seen in

FIG. 1. Photograph of anterior surface of liver showing irregular type of nodular cirrhosis following destruction of most of parenchyma. A portion of the right lobe, upper zone, is practically uninvolved.

the capsule strips with ease, leaving a smooth surface marked by small cysts. The left kidney resembles the right. The vessels and ureters are normal.

Adrenals: Normal.

Bladder: Is filled with dirty mud-colored urine. The mucosa is slightly injected.

Genitalia: Cervix is senile in type, endometrium is hemorrhagic and there is a small leiomyoma in the posterior wall.

Aorta: Presents numerous atheromatous plaques in the abdominal portion.

MICROSCOPIC EXAMINATION

Heart: A section of left ventricle is normal.

the muscularis and beneath a thickened serosa. No ulceration.

Kidneys: Many bile-stained hyaline and granular casts in the cortex. Glomeruli slightly thickened.

Uterus: Many large hemorrhages in endometrium and upper layer of myometrium which also shows much myofibrosis.

Ovary: Senile type.

Gall-Bladder: Marked chronic inflammation of mucosa and submucosa with heteroplasia of mucosal epithelium.

Liver: Widespread destruction of lobules with loss of architecture. Many sections contain no parenchyma but only proliferating bile ducts, mononuclear cells, stroma,

and blood vessels. Certain parts show regenerating liver cells in pseudo-lobule formation. The bile canaliculi are dilated with bile thrombi. The capsule of the liver is much wrinkled due to loss of substance beneath. The picture is typical of subacute "yellow atrophy" or necrosis of toxic origin with some repair.

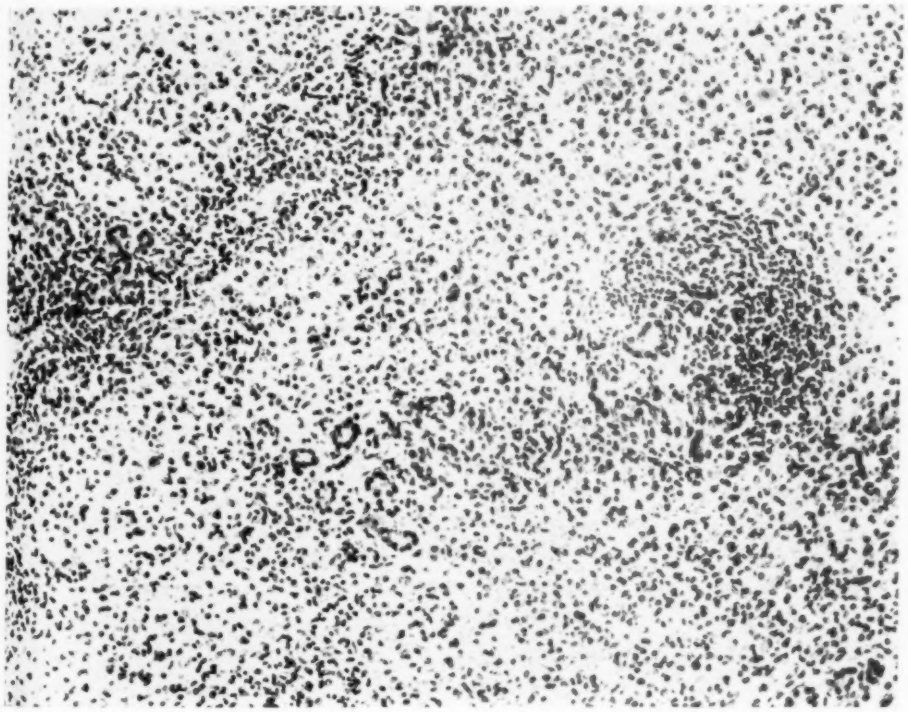

FIG. 2. Photomicrograph showing the loss of liver parenchyma, infiltration of lymphoid cells and proliferation of bile duct epithelium.

Microscopic Diagnosis: Subacute yellow atrophy of liver; chronic cholecystitis; acute pancreatitis; acute pneumonitis; endometrial hemorrhage.

DISCUSSION

Cinchophen. Cinchophen is phenyl-quinolin-carboxylic acid. It was introduced in therapeutics under the proprietary name "atophan" and is derived from quinolin carboxylic acid. Doebner and Giesecke in 1887 described 2-phenyl-quinolin-4-carboxylic acid. They prepared it by warming together pyroracemic acid, benzaldehyde and anilin in alcoholic solution.

Action. It stimulates the kidneys in such a way as to have a selective effect on the excretion of uric acid, which is increased considerably. The amount of ammonia and of total nitrogen in the urine is slightly increased during the action of cinchophen. Cinchophen does not increase the leukocytes, purin bases or the phosphoric acid. There is no evidence of increased formation of uric acid nor of any effect on deposited urates.

The above two paragraphs are taken from *New and Nonofficial Rem-*

edies, 1924 edition, published by the American Medical Association.

The clinical use of cinchophen has been based largely upon the fact that there is an increase in uric acid output after its administration. While the mechanism of this effect is not entirely clear there seems to be a selective action on renal epithelium since a diuresis is also produced. It has become, next to diet, the chief weapon in the treatment of gout. The drug and its derivatives have also an important analgesic effect and are antipyretics as well, features likely to attract clinical interest towards any therapeutic agent.

According to Rabinowitz[1] toxic jaundice and hepatolysis may result not only from atophan (cinchophen), but also from atophanyl and diiodoatophan. Atophanyl is a combination of the sodium salt of atophan and salicylic acid, while diiodoatophan contains 50.7 per cent iodine and has been used in Austria and Germany for cholecystography.

The toxic action of cinchophen has been thought due to the quinolin nucleus, consisting of the benzol and pyridin rings which yield the toxic, free benzol ring. Most individuals, fortunately, are not susceptible to the toxic effect of the drug. It is undoubtedly true that toxic jaundice will result only in the case of individual idiosyncrasy, but the fact remains that in spite of supposedly careful use of these compounds fatalities do occur. It is also true that serious symptoms may develop after withdrawal of the offending drug. Contraindications to use, such as nausea, vomiting or gastrointestinal symptoms, may not be present at all or come so late that they cannot be used as criteria of toxicity. Because of these facts cinchophen and its derivatives must be regarded as sources of danger and it would seem best to restrict their use when possible in favor of drugs which are less toxic.

Great importance must undoubtedly be given to the amount of glycogen in the liver cells at the time of cinchophen administration. There is undoubtedly a greater tendency to liver degeneration where there is malnutrition and a decrease in the glycogen content of the liver cells. As a result of this depletion, intoxications tend more readily to cause degeneration of the liver cells. Especially predisposed are alcoholics, pregnant women, and those who in the past have suffered from liver diseases associated with jaundice. It is important to remember that cases of chronic liver atrophy may suddenly present a picture of acute yellow atrophy, leading rapidly to death.

The dose or the duration of use of the drug will vary in individual instances—one developing toxic jaundice after as small a dose as 7 grains, others having a tolerance of several thousand grains taken during a period of years before intoxication occurs.

In 1922, Schroeder[3] described jaundice resulting from the use of cinchophen and published a review of seventeen cases. Since then the literature has shown many examples of fatalities from its use.

In 1929, Reichle[4] described two cases of toxic cirrhosis due to cinchophen resulting in death, and gave an excellent review of the literature since

1922. He found 47 reports of poisoning with 10 deaths.

Hitzenberger[5] cites the case of a young woman who died 10 days after diiodoatophan, administered for cholecystography. She had suffered from diabetes insipidus and occasional febrile attacks. A slight tenderness under the ribs suggested the possibility of gall-bladder disease, and cholecystography was undertaken.

Singer[6] also reported the case of a 50-year-old woman whose death took place after the use of diiodoatophan for cholecystography. Definite jaundice occurred the following day.

Langdon-Brown[7] observed fatalities after the use of atophan for rheumatism and stated that he knew of several others.

Anderson and Teter[8] reported a fatality in a woman of 48 years who had been taking oxyl-iodide capsules for arthritis.

Stacy and Vanzant[9] recorded the case of a woman of 52 years who took from one to three tablets of cinchophen daily for pain. She finally discontinued its use because of nausea and vomiting, but evidently too late, as she died one week later from acute yellow atrophy of the liver.

Rabinowitz[10] has recently reported seven additional cases of cinchophen poisoning, four of which were fatal. He quoted Dr. Leo Kessel as having seen thirteen cases of atophan poisoning. From conversations with various practitioners in eastern New York we have concluded that in the use of this group of drugs untoward symptoms are very frequently observed, and that there are many unreported fatalities.

A striking fact is the high proportion of fatal cases in women. Twelve of fourteen deaths occurred in females. The ages vary from 20 to 63. The influence of pregnancy and its frequent toxemias on the liver, the higher incidence of gall tract disease in women, and the more general tendency in women to disturbances of metabolism in later adult life, may all be factors in producing this sex preponderance.

The incidence of diffuse toxic necrosis of the liver—or, as it is more commonly but less properly called, acute yellow atrophy—has apparently increased in recent years, a fact attributed to the increasing use of various cyclic organic compounds, among which is the group concerned in our case.

The etiology is quite unknown but probably there is no specific cause since various forms of intoxication may closely simulate acute yellow atrophy, i.e., puerperal eclampsia, streptococcus septicemia, also poisoning with phosphorus, arsenic, nitrophenols, and even mushrooms. It is probably true, as Wells and Bassoe[11] state, that *any poison which does not directly cause death, but which causes a severe injury to the liver cells without at the same time destroying the autolytic enzymes, so that the cells die and undergo rapid autolysis, may produce a condition identical with or similar to acute yellow atrophy.*

Intracellular oxidations are probably affected in diffuse toxic necrosis, although fatty infiltration is more evident in the liver of phosphorus, chloroform and other poisonings. The fatty change is taken to be evidence of inhibition or destruction of oxidizing enzymes, the autolytic enzymes

being left free to act.[12] The ability of sugar to protect the liver from poisons such as phosphorus and chloroform seems to depend on its furnishing easily oxidizable material to cells with lessened oxidative capacity (Simonds[13]). Ervin,[14] however, regards the protective action of carbohydrate as due to the liver glycogen which protects the protein-fat emulsion of the protoplasm from the action of acids. Nevertheless with the liver destruction carbohydrate tolerance is reduced (Bodansky[15]).

Stewart, Vining and Bibby[16] emphasize the fact that acute yellow atrophy occurs more often after poisoning with picric acid, trinitrotoluene, dinitrobenzene, and aromatic arsenicals, and since the benzol ring is the only common component in these compounds, and is also present in cinchophen, its responsibility is strongly suggested.

In the literature dealing with poisonings of various kinds the word idiosyncrasy is frequently encountered. This term implies that a person has some peculiar constitutional susceptibility to the substance in question, a condition incapable of more concrete definition and hence probably covering a multiplicity of contributing factors. Minute analysis of clinical and pathological data may often give a more objective basis for the toxic state. In our case, for instance, at necropsy a very marked chronic cholecystitis was present although no gall-stones were found. This condition may have been present for years and possibly was responsible for the use of drugs for the "shoulder" pains which she had experienced. There is no definite evidence that gall-bladder disease per se affects liver function, but it is conceivable that such contiguous lesions may render the liver less resistant to toxins which have an affinity for it.

Cinchophen or atophan and its related compounds are sold in most drug stores. Theoretically they are supposed to be procurable only by prescription but it is quite feasible for any one to purchase them without a physician's written order. This of course leaves open the possibility of abuse of the drug by the laity, especially since the bottles in which the powders or tablets are put up have no precautions printed on the labels. The physician is probably to blame in large measure for most cases of cinchophen poisoning since he is the proper person to warn his patients about the dangers of any form of medication he prescribes.

One manufacturer of this group of remedies gives ample warning to the profession about their contraindications. In a pamphlet[17] sent out to physicians at regular intervals by this company the following cautions are given: "Discretion should be exercised in the use of this drug with individuals suffering from hepatic and biliary dysfunction, especially as it is evidenced in the elderly and poorly nourished patient; yet, if progressive degeneration of these organs is neither known to be present nor reasonably to be suspected, clinical observers believe that this form of medication need not be withheld, more especially if a diet rich in carbohydrates be provided and maintained paralleling the treatment. The use of oxyl-iodide compound is not recommended during pregnancy or for alcoholics. The drug should be at

once discontinued if any of the following symptoms are observed: loss of appetite, nausea, vomiting, tenderness over the liver or in the gallbladder region, icteroid tint to the sclera or skin, urticarial rash, itching of the skin, swelling of the lips, tongue or face. The appearance of albumin, casts, or bile in the urine should be an indication for the interruption of the administration of the drug."

It would seem that the above constitutes a very genuine effort upon the part of the manufacturer to make the physician realize the dangers of the cinchophenic compounds. Certainly it behooves the latter to acquaint himself thoroughly with their powers for evil before prescribing them for his patients. The dispenser, on the other hand, should be required to indicate on the labels of the containers the dangers of the unguided use of the contents.

SUMMARY

1. Cinchophen or atophan and its related compounds are capable in susceptible individuals of causing toxic symptoms which may eventuate in the so-called yellow atrophy of the liver.

2. A case is reported of subacute yellow atrophy in a woman aged 68 years, who in the previous two months had taken for arthritic pains about 263 grains of cinchophen and 75 grains of oxyl-iodide-phenylcinchoninic acid.

3. The benzol ring is a common component of this group of remedies and its responsibility for the toxicosis is strongly suggested.

4. Physicians prescribing these drugs should become familiar with their dangers and warn patients against using them without direction.

5. A large majority of the cases of poisoning occur in women.

6. In our case a concomitant cholecystitis of marked degree was present.

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Migrating Pneumonia*†

Certain Mechanical Factors in Its Production, Prevention, and Treatment

By William B. Faulkner, Jr., M.D., Aime N. Fregeau, M.D., and Edward C. Faulkner, M.D., *San Francisco, California*

A CLOSE study of postoperative massive collapse of the lung (pulmonary atelectasis) indicates its marked similarity to pneumonia. These two conditions have many characteristics in common and, from the study of atelectasis, we may draw certain deductions relative to pneumonia.

As observed by Norris and Landis,[1] "practically every case of pneumonia spreads to some extent. In some cases it slowly extends spreading from lobe to lobe by contiguity; in others the process apparently develops afresh at different points in the same or the opposite lung", and, "in double pneumonia, both bases may be affected simultaneously or the apex of one lung and the lower lobe of the opposite lung may be involved". This migrating or wandering pneumonia, which moves from place to place within the same or the opposite lung, also has been designated as "creeping", "progressive", and "extending" pneumonia.

We believe that migrating atelectasis and migrating pneumonia are attributable to the same factors. This conclusion is reached by studying the changes in the position of the abnormal signs after the patient has changed from one posture to another. Pneumonia, as well as atelectasis, migrates to definite areas, in accordance with the principles of "internal drainage",[2] i.e., the spilling of pus or secretion from place to place within the same or the opposite lung, plugging bronchi, obstructing air flow, and causing infection of previously uninvolved areas. The spilling is on a mechanical basis. It depends upon the amount and viscosity of the intrabronchial pus, the posture of the patient, the course of the bronchial stems, and the relative position of the various bronchial openings. (Figures 1, 2, and 3)

The changes within the bronchi are influenced further by the virulence of the organisms within the intrabronchial exudate; but there will be no spilling or migration in the absence of excess intrabronchial secretion.

Bronchoscopic examinations support these deductions and show that thick

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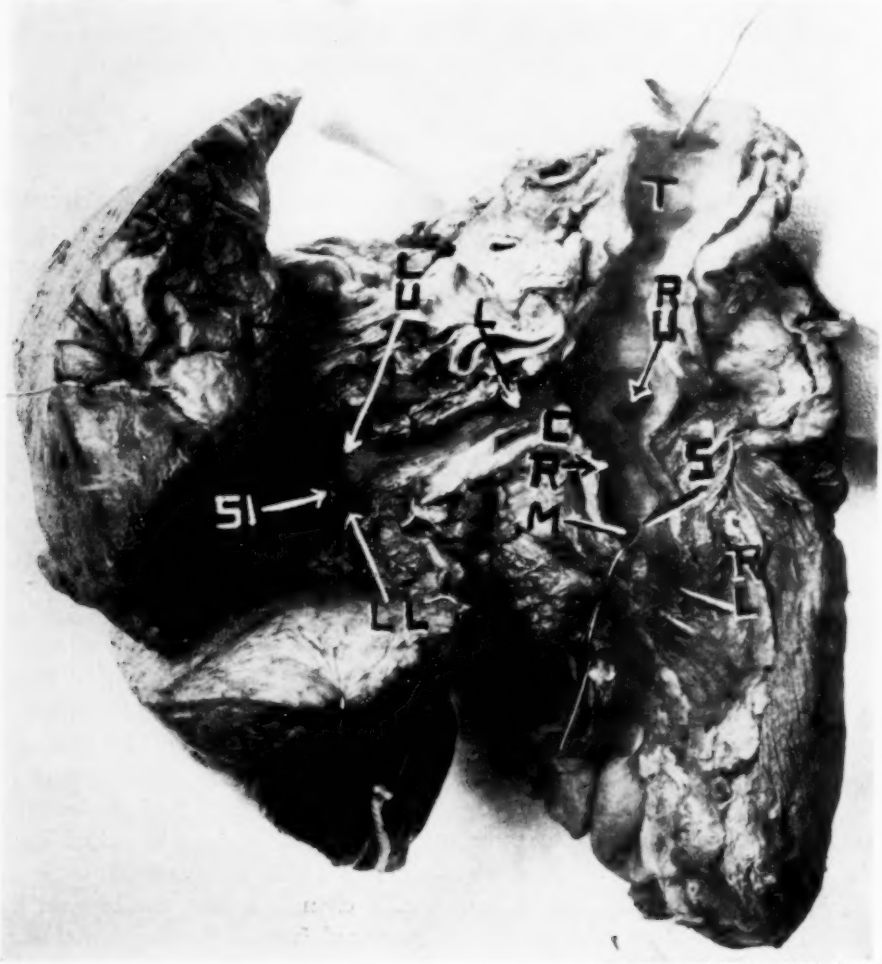
†From the Department of Surgery, University of California Medical School, San Francisco; Department of Medicine, French Hospital, San Francisco; and Department of Thoracic Surgery, St. Mary's Hospital, San Francisco.

pus gravitates less readily than thin watery material. Should thick sticky pus be dislodged from the original site of a pneumonic area, it is likely to plug a large bronchus, shut off air flow from a great portion of a lobe or an entire lung, and give signs of lobar pneumonia over a new site. Thinner material spills with greater ease, runs deeply into the lung, and either plugs or fills one or several small minor bronchi to produce signs of bronchopneumonia. Such migrations of both bronchopneumonia and lobar pneumonia owe their origin to the same cause, namely, internal drain-



—*Courtesy of Jr. Am. Med. Assoc.*

FIG. 1. Specimen illustrating the anatomy of the tracheobronchial tree, the free communication between the various bronchi, and the ease with which the material may spill from one to the other. Note the position of the right upper lobe bronchial opening (RU) almost directly opposite the bifurcation of the trachea (C). L- Left main bronchus dividing into the left upper (LU) and left lower (LL). S1- septum between these two bronchi. R- right main bronchus divided by the septum (S) into the middle (M) and the lower lobe bronchus (RL).

age. Any apparent difference in the two is attributable to the varying viscosity of the intrabronchial secretion and the size of the plugged and infected bronchi. One can predict even the sites to which pneumonia will migrate for these are determined by the posture of the patient.

For example, let us consider the probable sites of migration of a pneumonia beginning in the right upper lobe. When the patient lies flat upon the affected side, there is little opportunity for spilling or migration to other lobes. (Figure 4) If he is flat upon his back instead of upon his side, the anterior portion of the upper lobe may escape, but this is not always the case. The small bronchi to the anterior and posterior portions of the upper lobe are in extremely close relation and pus can extend readily from one

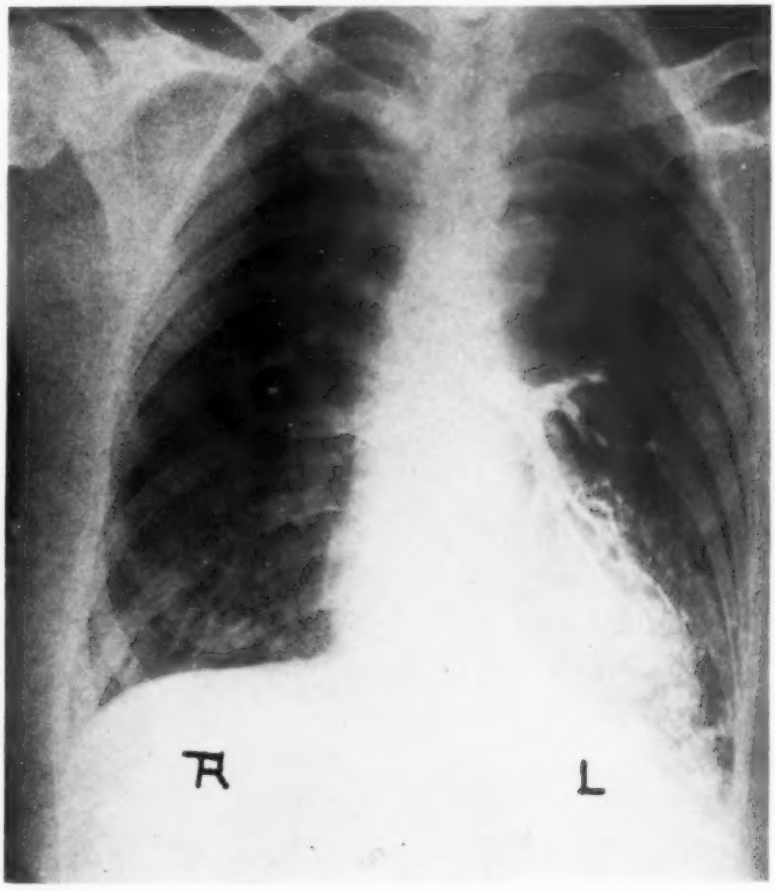


FIG. 2. Iodized oil roentgenogram to illustrate the facility with which intrabronchial material can migrate by "internal drainage". The oil was introduced without the use of any type of anesthesia with the patient leaning slightly towards the left. Note the absence of oil in the right lung. Compare with plate 3.

to the other. (Figures 5 and 6) Should the patient be placed in the semi-Fowler or sitting position, the spilling of pus from the upper lobe is facilitated. This material gravitates along the floor of the right main bronchus to the first available opening, small amount of secretion plugging the bronchus and the comparatively large area over which the abnormal physical findings are elicited. Every change in the position of the patient leaves him liable to the spilling of pus and the consequent migration of the pneumo-

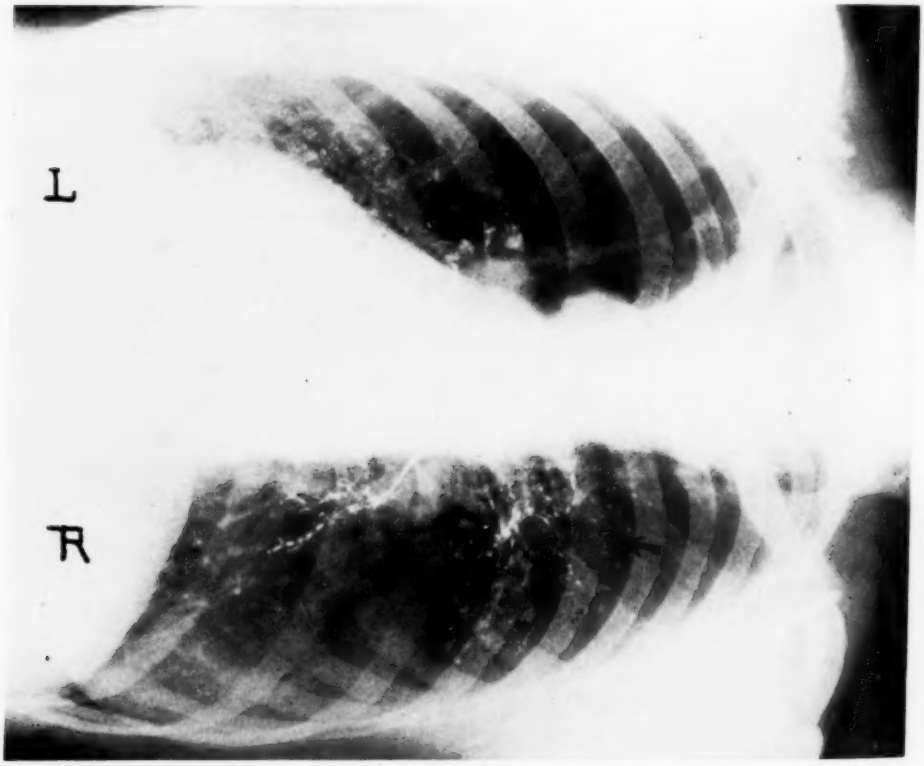


FIG. 3. Same patient as in figure 2. The oil spilled from the left lung into the right when the patient lay upon the right side. There was no cough associated with this spilling. It was caused by the change in the posture of the patient.

which is the posterior minor bronchus of the lower lobe. By plugging or filling this small bronchus, it produces abnormal findings at the area below the angle of the right scapula.

All clinicians are familiar with the frequency of pneumonia at this site, but attention should be called to the striking disproportion between the nia. The progression of the disease into the sound lung when a position on the unaffected side is assumed, should be sufficient evidence of the influence of posture upon migration. The high position of the right upper lobe bronchus almost directly opposite the bifurcation accounts for the spread of pneumonia from the right upper to the

left lower lobe and vice versa. (Figure 7)

We have observed very closely the changes in the physical findings following alterations in the posture of patients who have pneumonia. Râles occasionally appear at new areas and there is an interference with the inflow and outflow of air at this particular region. Later there is a change in the percussion note. More frequently there is hyperresonance over the area to which the pus has spilled but the breath sounds are markedly reduced or completely absent. This is exactly what one finds in the case of an intrabronchial foreign body. The signs are caused by the obstruction of the bronchus and the trapping of air resulting in the production of an obstructive emphysema. The strongest argument in favor of the mechanical

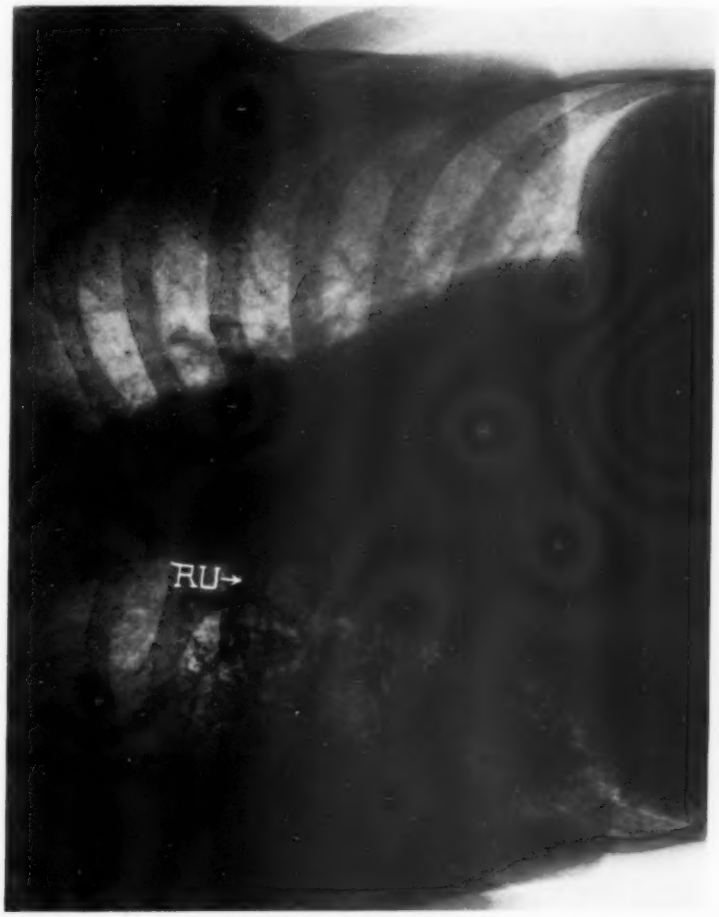


FIG. 4. Iodized oil injection of the right lung demonstrating the horizontal course of the right upper lobe bronchus (RU) and the difficulty of pneumonia migrating from this area to new sites when the patient lies upon the affected side.

production of this migration is that the signs change with a rapidity equal to those produced by an intrabronchial foreign body. Following the absorption of the air which is trapped beyond the plug of pus, an atelectasis ensues, infection sets in, and if the condition is not corrected, a true pneumonia of the migratory type becomes established at this site.

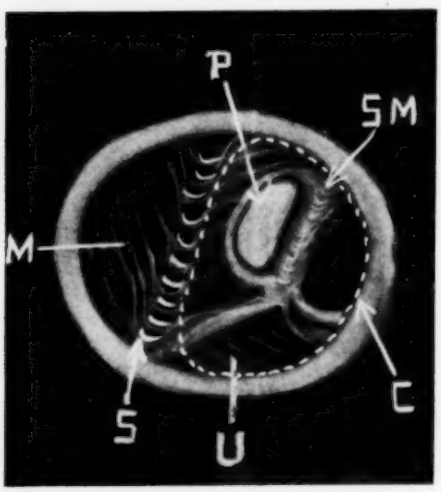


FIG. 5. Diagrammatic sketch of the bronchoscopic appearance of the right upper lobe bronchus. S-septum separating the upper lobe bronchus (U) from the main stem bronchus (M). Note the nearness of the minor divisions (P and C). This close proximity permits material to migrate from one to the other. SM-minor septum.

The acceptance of this mechanical factor in the production of migrating pneumonia enables us to adopt measures not only to prevent but also to treat the condition. The patient can be kept in such a position as to lessen the likelihood of spilling to new areas. Nevertheless, even in these instances, there may be a welling up of pus to such an extent that there is some overflow to the dependent and accessible regions.

Prevention of migration really rests upon the removal of the intrabronchial pus. This often can be attained through expectoration. It is facilitated by the administration of expectorants and a saturated solution of potassium iodide which lessens the viscosity of the secretion. Steam inhalations serve the same purpose, while inhalations of pure carbon dioxide gas so widen the bronchi that the evacuation of the intrabronchial material is possible.

With all these methods of removal, the posture of the patient should be such that the material will drain out of the lung rather than deeper into it. These postures are extremely variable and depend on the site of the pneumonia. Atropin, which tends to thicken secretions, is contraindicated for these patients because it interferes with expectoration.

Should it be noted that secretions are spilling and are not evacuated following cough and postural exercises, bronchoscopic removal of the secretion, and bronchoscopic treatment of the affected regions should be instituted before the onset of atelectasis and subsequent pneumonia. In trained hands, the bronchoscopy can be done in from one to two minutes under local anesthesia without particular discomfort to the patient.

These mechanical principles are offered as adjuncts in the management of patients with pneumonia without any intention of minimizing the value of the other general therapeutic measures of proven worth.

CONCLUSIONS

1. Postoperative massive collapse of the lung (pulmonary atelectasis) has many characteristics in common with bronchopneumonia and lobar

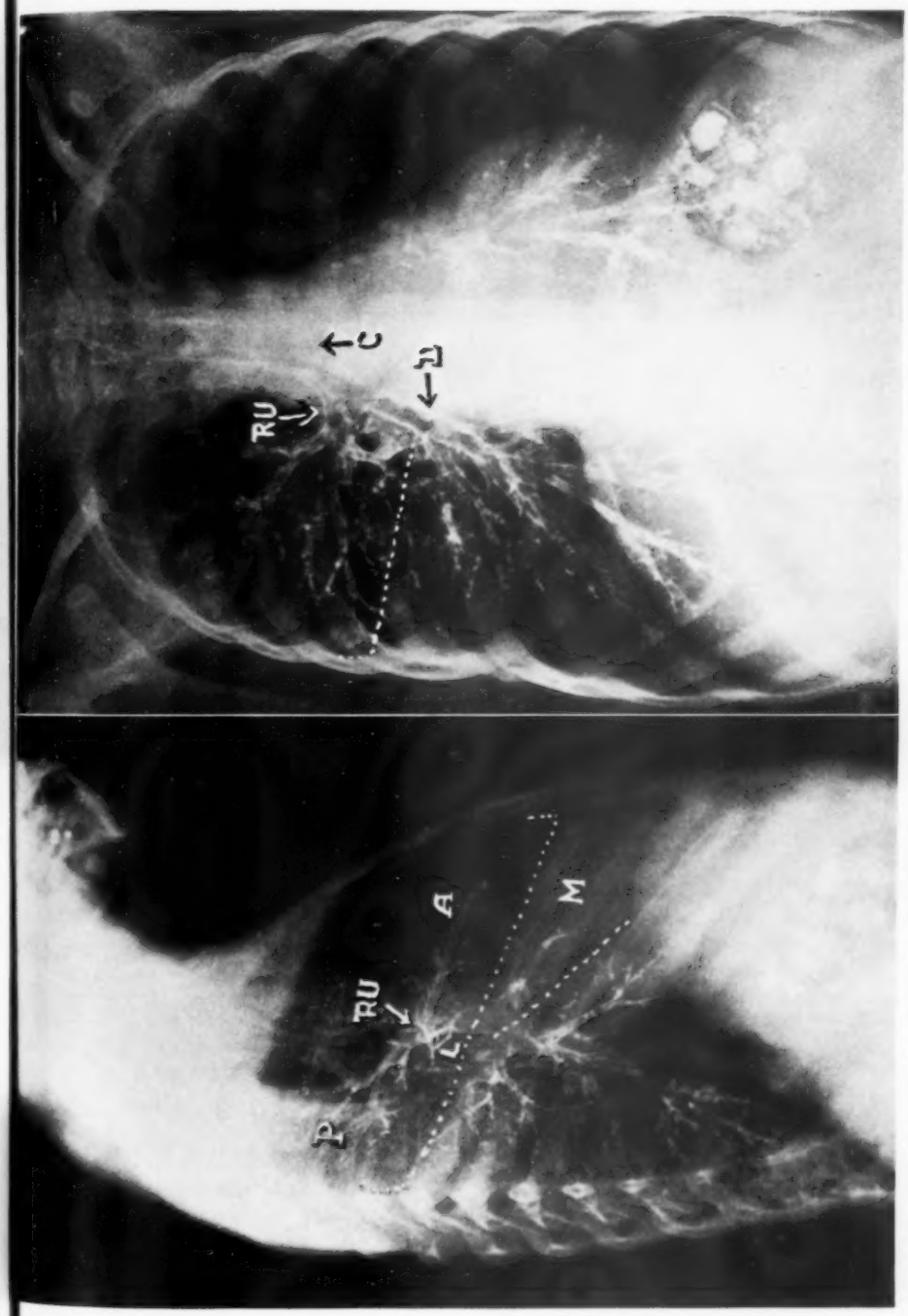


FIG. 6. Iodized oil injection of the right lung to demonstrate the close relationship of the branches of the upper lobe bronchi. RU- right upper lobe bronchus dividing into its anterior (A), posterior (P), and lateral branches (L). M- middle lobe; C- carina (bifurcation of the trachea); D- point of origin of the middle and lower lobes.

pneumonia. Both show strong tendencies to migrate to identical areas following similar changes in the posture of the patient.

2. Evidence is offered to show that the migrations in pneumonia are on a mechanical basis. They are dependent on the original site of the pneumonia, the posture of the patient, the intrabronchial anatomy, and the amount and viscosity of the intrabronchial pus.

3. This whole problem is intimately connected with the mechanism of "internal drainage", i.e., the spilling of secretion from place to place within the same or the opposite lung.

4. Thin secretion spills deeply into the lung, plugs small scattered bronchi and produces a migratory bronchopneumonia. More viscid material gravitates less readily. It leads to obstruction and infection of the major

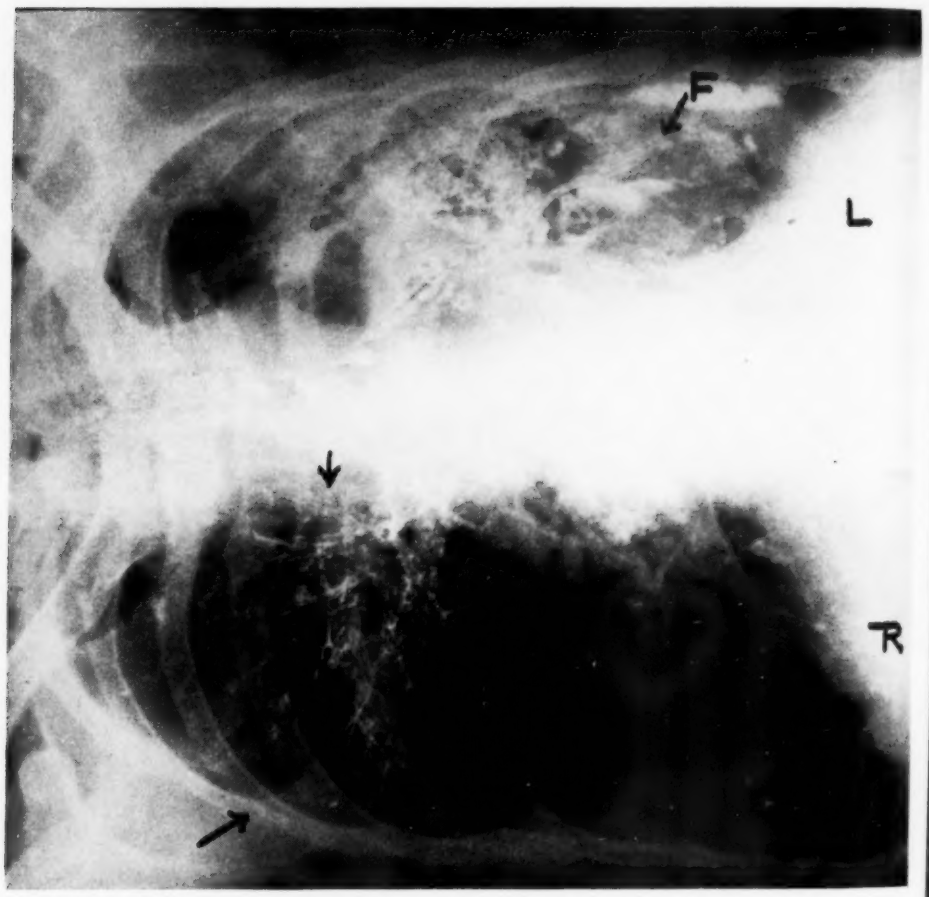


FIG. 7. Iodized oil introduced into a left lower lobe bronchial fistula (F) without the use of any type of anesthesia spilled across the bifurcation into the right upper lobe when the patient lay upon the right side. The facilities for the migration of secretion from the left lower to the right upper lobe are demonstrated also in figure 1.

bronchi resulting in a migratory lobar pneumonia.

5. The administration of expectorants, the use of saturated solution of potassium iodide to lessen the viscosity of the secretions, and the adoption of proper postures offer a means of evacuating the bronchi and preventing the internal drainage which is responsible for the production of migrating pneumonia.

6. The bronchoscopic removal of the intrabronchial exudate is to be recommended whenever the patient fails to respond promptly to the other therapeutic measures.

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Maintenance Dosage of Liver Extract in the Treatment of Pernicious Anemia*†

By Paul J. Fouts, M.D., and L. G. Zerfas, M.D., *Indianapolis, Indiana*

In presenting data relative to the maintenance dosage of liver extract or other substances potent in the treatment of pernicious anemia, it is necessary to define and state the requirements which this term implies. Beebe and Lewis[1] have clearly defined these requirements in a recent report of a large series of cases observed at the Thorndike Memorial Laboratory and at the Boston City Hospital. They stated that, "although the level of the red blood cells and hemoglobin serves as one important guide to the amount of therapeutic material necessary for the maintenance of health, there are other aspects of each case that should be recognized as important criteria in determining the amount of liver or potent substitute that should be taken. These other matters pertain to the patient's habits, symptoms and physical signs, the presence or absence of complications, and the detailed histology of the blood itself."

There is much information relative to the course of this disease before the advent of liver, kidney, and stomach therapy with which to compare the results obtained following the administration of effective therapeutic substances over prolonged periods of time. It is essential that "prolonged periods of time" be emphasized, because of the occurrence of spontaneous remissions, the duration of which is known to vary considerably in the same and in different patients.

It has been a common experience to see patients attempt to regulate their own dosage. Many times both patient and physician are misled as to the determination of the proper maintenance dosage, because prolonged periods are often required to determine the effects of an increased or decreased daily amount of potent substance. The psychology of these patients under treatment and the insidious nature of the disease are other factors that constitute serious obstacles in their proper treatment. It is obvious that frequent observations relative to the clinical aspects of the disease and to the state of the blood are imperative at frequent intervals for the proper management of the patient.

We have selected, from a series of 150 cases treated, fifty-nine patients with typical pernicious anemia, on the basis of the duration of treatment (none less than one year), frequency of observations, and consistency with

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†From the Lilly Laboratory for Clinical Research, Indianapolis City Hospital, and the Department of Medicine, Indiana University School of Medicine.

which they ingested the prescribed amount of liver extract. The average duration of treatment of these patients was thirty-six months, ranging from twelve months (two cases) to fifty-seven months. At the beginning of treatment, fifty-seven of the fifty-nine patients were admitted to the hospital in severe relapse, and afterwards were released to the "Out-Patient Department", where they have continued treatment under our personal observation and management. The two remaining patients were admitted to the "Out-Patient Department" while in a remission. As a rule these patients were regular in attendance, reporting at monthly intervals, at which time they were supplied gratis with a sufficient amount of Liver Extract No. 343* to last until their next visit. Under these circumstances, the regularity of their visits was quite imperative. Occasionally certain patients attempted to make the monthly quota of extract do for two months or longer and others omitted therapy altogether until it became obvious to them that they needed further treatment.

The average red blood cell counts, percentages of hemoglobin, and daily amounts of extract which they consumed were computed in each case studied, beginning with the time that the red blood cell count and hemoglobin reached normal levels. It is regrettable that each individual case cannot be presented in full detail as to the blood determinations and clinical findings, as there are many points of interest which are not recorded or which are obscured by the general averages. The daily amount of potent extract to maintain the blood at normal and to keep the health of the patient in a satisfactory state was calculated over a period of not less than one year. In the majority of instances, either smaller daily amounts had been taken previously for a year or more and found insufficient, or larger daily amounts were reduced for a similar period of time without appreciable changes in the blood or in the health of the patients. The average maintenance dose of potent liver extract, so computed, represents the minimum daily amount as determined in this series of patients during an average period of thirty-six months. We have used the same lower limits of normal as those stated by Beebe and Lewis—4,500,000 red blood cells per cubic millimeter and 85 per cent hemoglobin. The hemoglobin was determined by the Newcomer method. There were a few cases in which the average percentage of hemoglobin was slightly less than 85 per cent which were included in the normal group, since the red blood cell counts and the general health of the patients were satisfactory.

An analysis of the series of fifty-nine patients treated showed that thirty-eight (64.4 per cent) maintained normal red blood cell counts and hemoglobin percentages while taking the daily amount of extract derived from three hundred grams of liver, or less. These patients were classified as Group I. The twenty-one remaining cases (35.6 per cent) did not maintain normal red blood cell counts and hemoglobin percentages while taking the

*The liver extract was supplied by Eli Lilly and Company.

daily amount of extract derived from three hundred grams of liver and were classified as Group II.

In table 1 the patients composing Groups I and II have been further subgrouped as to the average daily amount of extract taken. The average

tract derived from 400 and 600 grams of liver. These patients had previously been given the amount of extract derived from 300 grams of liver, but their blood and hemoglobin either did not reach normal or was not maintained at normal for any length of time

TABLE I

The data in table 1 show the number of patients who did or did not maintain normal red blood cell counts and hemoglobin percentages while taking various daily amounts of potent liver extract. The amount of liver extract is expressed in terms of the number of grams of whole liver from which it was derived, as it is generally considered that 25 to 30 per cent of the active principle contained in liver is lost by fractionation.

	GROUP I				GROUP II		
	LESS THAN 100 GRAMS	100 GRAMS	200 GRAMS	300 GRAMS	400 GRAMS	600 GRAMS	300 GRAMS†
Number of cases	3	6	10	19	4	3	14
Average age in years	57	55.1	53.7	55.5	58.2	44.3	59.5
Average number of red blood cells per cubic millimeter (in millions)	5.32	4.85	5.01	4.84	4.92	4.83	3.92
Average hemoglobin percentage	89.2	82.5*	86.7	85.6	86.2	88.9	77.2
Average amount of liver extract (in grams)	60	100	200	300	400	600	328

*Three patients who had normal red blood cell counts, but whose hemoglobin percentages were below 85 per cent, were considered essentially normal, since their general health was in a satisfactory state.

†Two patients in this group received the daily amount of liver extract derived from six hundred grams of liver.

red blood cell count, percentage of hemoglobin, and the average age of the patients in each subgroup have been determined. It can readily be seen from an examination of this table that there is a great variation in the daily amount of extract ingested capable of maintaining the blood and hemoglobin at normal levels over a period of time greater than that usually observed in spontaneous remissions. Seven of the patients in Group II reached and maintained normal red blood cell counts and hemoglobin levels while taking the daily amount of extract on this dosage. The remaining fourteen patients in Group II ingested inadequate daily amounts of the extract when they took regularly the amount derived from 300 grams of liver. Seven of the fourteen patients still living are receiving large daily amounts of the extract, but sufficient time has not elapsed to evaluate the dosage for inclusion in this paper. Since thirty-eight of the patients (64.4 per cent) maintained normal blood counts and hemoglobin percentages on the daily amount of extract derived from 300 grams of liver and less, it is still neces-

sary to question why twenty-one (35.6 per cent) were unable to reach or maintain normal blood levels while taking regularly the daily amount of extract derived from 300 grams of liver.

TABLE II

The data presented in this table correlate the blood and the clinical aspects of the fifty-nine patients treated with liver extract for an average period of thirty-six months, as separated into Groups I and II.

	GROUP I	GROUP II
Number of patients	38	21
Average age in years, on admission	55.1	58.1
Average red blood cell count in millions per cubic millimeter	4.92	4.19
Average hemoglobin percentage	85.6	80.9
Average daily amount liver extract (in grams liver)	223	381
Percentage of patients with moderate to advanced arteriosclerosis	47.2	71.4
Percentage of patients with chronic infections	2.6	28.6
Percentage of patients with noninfectious complications	18.4	52.4
Percentage of patients who had moderate to advanced central nervous system involvement at the onset of treatment	34.2	66.6
Number of patients who developed central nervous system involvement while on liver extract treatment	3	2
Number of patients who developed central nervous system involvement and later improved	1	0
Number of patients with moderate to advanced central nervous system involvement who improved during treatment	4	1
Number of patients with moderate to advanced central nervous system involvement who had an increase in this involvement during treatment	1	10
Number of patients who died during treatment	0	7

In table 2, the average red blood cell count, hemoglobin percentage, and the daily amount of liver extract ingested have been correlated with the clinical aspects of the patients as previously classified (Groups I and II). The thirty-eight patients in Group I maintained an average red blood cell count of 4.92 million and percentage of hemoglobin of 85.6 per cent, while taking an average daily amount of extract derived from 223 grams of liver. This average daily amount we consider to be the minimum. The twenty-one patients in Group II maintained an average red blood cell count of 4.19 million and percentage of hemoglobin of 80.9, while taking daily the average amount of extract derived from 381 grams of liver. While this average daily amount was much greater than that recorded for Group I, it is still far below the minimum for this group and, therefore, inadequate. The average age of the patients in Group II was only slightly greater than that of Group I. In comparing the clinical aspects of these two groups, it is inter-

esting to note that, despite the slight difference in the average ages, the patients of Group II showed a much higher incidence of arteriosclerosis. The usual clinical means for determining arteriosclerosis were employed, such as digital palpation of the peripheral arteries, ophthalmoscopic examination of the retinal vessels, and blood pressure determinations.

The percentage of complications of an infectious and a noninfectious nature, separate and apart from the central nervous system involvement, was much greater in Group II than in Group I. These facts are significant, as the noninfectious complications include those degenerative conditions commonly seen in cases with advanced arteriosclerosis. In many instances the infectious processes involved the urinary tract, and some of these complications were secondary to the bladder disturbances resultant from advanced central nervous system involvement.

The incidence of central nervous system involvement on admission to the hospital was 34.2 per cent for Group I and nearly twice this percentage (66.6 per cent) for Group II. Therefore, it cannot be said that the greater incidence of central nervous system involvement in Group II occurred because of an insufficient amount of liver extract ingested while under treatment or because of a failure of the blood to reach or maintain a normal level. It can be said, however, that the number of patients whose central nervous system involvement advanced while under treatment was much greater in Group II (ten patients) than in Group I (one patient). Three patients in Group I and two patients in Group II developed central nervous system involvement for the first time while under treatment, and only one of these patients improved (in Group I) while under treatment.

Four of the total number of patients in Group I, who had central nervous system involvement present at the onset of treatment, improved during liver therapy, in contrast to one patient in Group II. Many patients showed improvement of the minor signs and symptoms of central nervous system involvement while taking potent fractions of liver, but in this series we have considered only those cases showing moderate to advanced lesions, as interpreted by the clinical findings. Repeated clinical observations indicate that there are quiescent and actively progressive phases of the central nervous system involvement which may be recognized from time to time. During one of these active phases it is common to see the level of the red blood cells decrease; usually the decrease in the percentage of hemoglobin is much less, proportionately. Often large amounts of liver extract ingested daily (that derived from 1000 to 1200 grams of liver) will not be sufficient to cause the blood to return to normal or to prevent the progress of the central nervous system involvement at that time. During the entire period of observation, seven of the fifty-nine patients died while under treatment. These deaths occurred in Group II, while there were no deaths in Group I. All of the seven patients who died had advanced central nervous system involvement.

The data in table 2 indicate that

those patients with a higher incidence of complications, arteriosclerosis, and moderate to advanced central nervous system involvement (Group II) required, on the average, a greater daily amount of the active principle in liver to keep the blood and color index near normal. These findings are in accord with those reported by Beebe and Lewis.

An examination of the individual patients shows that an acute exacerbation of any or all of the above complications may lead to a severe relapse, even though the blood has been maintained at normal levels for a prolonged period of time while they are taking a given daily amount of liver extract. Occasionally, and for no apparent reason, relapses develop while they are taking the daily amount of potent extract which has maintained the blood and the state of their health at normal for as long as four and one-half years. Fourteen of the fifty-nine patients developed relapses some time during the period of observation, because of the omission of therapy or because of a reduction in the daily amount of liver extract. The time required to develop a relapse under either circumstance varied from two to eighteen months. In three cases more than one relapse occurred because of the omission of therapy. The length of time required to develop a relapse in the same patient varied from two to twelve months. Often a decrease in the hemoglobin percentage preceded, by several months, a reduction in the number of red blood cells previous to a relapse. However, a decrease in the number of red blood cells does not always follow, as the percentage of hemoglobin has been observed to return to normal while the patient was taking the same amount of potent extract. It would seem advisable, under such circumstances, to administer large doses of iron, as recommended by Minot and his associates.

It is reasonable to believe that a relapse is conducive either to the development of or to the exacerbation of already existing complications seen in this disease, thereby establishing a vicious cycle. Therefore, it is imperative that the blood and the clinical condition of the patient be observed closely at frequent intervals. In the presence of or at the onset of such a cycle, the daily amount of liver extract should be increased sufficiently to, at least, maintain the blood of the individual patient at a normal level. If for any reason the daily administration of large amounts of liver extract by mouth is not feasible during this time, the parenteral use of liver extract is indicated.

Conclusions

1. Fifty-nine patients with pernicious anemia were treated with Liver Extract No. 343 by mouth for an average period of thirty-six months.

2. In Group I, thirty-eight patients (64.4 per cent) maintained normal red blood cell levels and percentages of hemoglobin, while taking the daily amount of extract derived from 300 grams of liver or less (average 223 grams).

3. In Group II twenty-one patients (35.6 per cent) did not maintain an average normal red blood cell count or hemoglobin percentage, while taking the daily amount of potent extract derived from 381 grams of liver.

4. The maintenance dosage of liver extract varied in different patients and in the same patient at different times.

5. The incidence of infectious and noninfectious complications, arteriosclerosis, and moderate to advanced central nervous system involvement was greater in Group II than in Group I.

6. The number of cases which showed an increase of the central nervous system involvement while under treatment was greater in Group II than in Group I.

7. Seven patients with advanced central nervous system involvement in Group II died while on treatment, and no patients in Group I died.

8. In the presence of complications, both the blood and the clinical aspects of the patient should be observed closely, and, under any circumstances, amounts of potent material sufficient to maintain the blood at a normal level should be administered.

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Cardiospasm with Associated Arthritis*

By John H. Fitzgibbon, M.D., F.A.C.P., *Portland, Oregon*

MANY etiological and contributing factors have been mentioned in the literature of arthritis, but cases in which the condition is associated with esophageal obstruction must be relatively rare.

For five years, I have had under observation and treatment a patient in whom cardiospasm and arthritis are intimately associated. As symptoms of arthritis have at times accompanied the appearance of difficulty in swallowing and have improved after dilatation of the stenosis, it seems worth while to report the case as one in which there appears to be an intimate etiological relationship between esophageal obstruction and arthritis.

Case Report

Mrs. L. S. B., age thirty-one, was first seen May 4, 1927, in consultation with Dr. Frank McCauley and Dr. Wilson Johnston. She gave a history of cardiospasm of twenty years' duration. The stricture had not been dilated since 1919. As the result of marked obstruction and difficulty in swallowing, she had lost a great deal of weight. Her chief complaint, however, was generalized arthritis, on account of which she was confined to bed.

In June 1926, she had been very ill with pneumonia, and had been in bed for several weeks. Painful swelling of the feet and ankles appeared at that time. Following a diagnosis of pulmonary tuberculosis, she went to Arizona, where her chest condition improved and the lesion was pronounced arrested. Arthritis of the finger joints and wrists developed in October and November 1926. Four infected teeth were extracted at that time. In January and February 1927, swelling and pain in the joints increased and she returned to Oregon in March with her shoulders, knees, hips, wrists, ankles, and finger joints involved. She was unable to walk and was confined to bed.

Her tonsils had been removed in 1919, but a small amount of tonsillar tissue remained and was removed by Dr. Johnston, May 5, 1927.

Difficulty in swallowing had gradually increased over a long period of time and she was extremely weak. A large amount of mucopurulent, blood-streaked material mixed with food was frequently regurgitated.

Physical examination was negative except for generalized arthritis with swelling.

Laboratory findings were as follows: Urinalysis, negative. Hemoglobin, 89 per cent. Red blood cells, 4,704,000. White cells, 8,700. Polymorphonuclears, 64 per cent. Small lymphocytes, 24 per cent. Large lymphocytes, 2 per cent. Coagulation time, 7 minutes. Blood Wassermann, negative.

X-ray examination of the esophagus showed a markedly dilated esophagus with obstruction at the cardia. (Figure 1)

It was hoped that her general condition could be improved by relieving the esophageal obstruction. Several attempts were made, using the Sippy air bag dilator introduced over a piano wire guided by a previously swallowed silk thread. It was possible to introduce the bag into the stricture, but inflation was not followed by improvement, for the bag tended to slip out of position. Fluoroscopic examination while the bag was being inflated showed that as the

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bag filled with air from the upper end it slipped upward into the esophagus and out of the stricture. As the esophagus was greatly dilated, there was room for the flexible shaft of the instrument to bend laterally and permit the bag to slip upward. The instrument was then modified[1] so that air entered from both ends simultaneously, and no difficulty was experienced in successfully dilating the stricture.

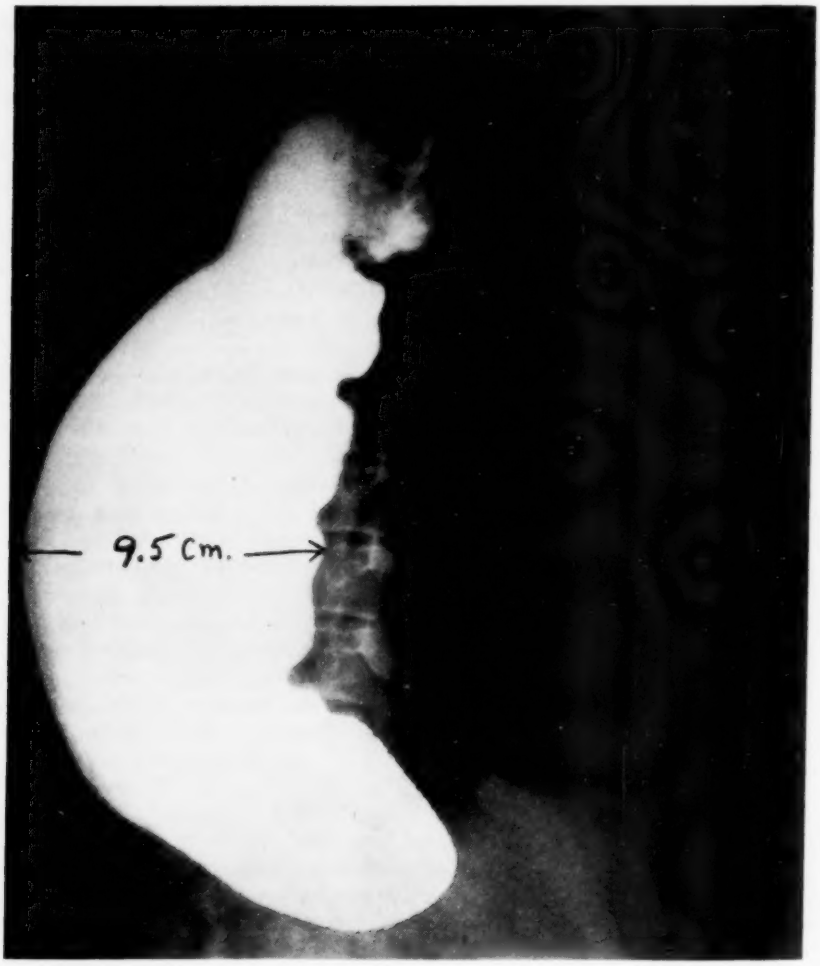

FIG. 1. Dilated esophagus due to cardiospasm.

The failures with the original dilator consumed a great deal of time. She was brought to the office for treatment and did not wish to make the trips often because of the inconvenience and the pain in the joints. It was necessary to carry her to and from the automobile. During this period she received quartz light and diathermy treatments from Dr. W. D. Lockwood. The esophagus was lavaged each evening, in the hope of relieving the local inflammation due to retention of food and secretions.

After successful dilation with the modified dilator, July 6 and 15, 1927, there was very

little difficulty in swallowing, and improvement in the arthritic symptoms began. Improvement continued and in September she was able to walk without pain. Her weight and general condition improved at the same time. She has experienced very little difficulty since. She has reported for treatment off and on, especially when difficulty in swallowing develops.

In January 1931, swelling and pain in the joints of the right hand and foot, reappeared, associated with difficulty in swallowing. Following satisfactory dilation of the cardia, these symptoms cleared up.

On November 3, 1931, she reported that she was four months' pregnant. As there was some difficulty in swallowing, and it was feared that this might increase during the remaining months of her pregnancy, her physician was consulted and the cardia was dilated with moderate pressure. On March 25, 1932, she returned, having passed through a normal pregnancy and delivery, but complained of a return of her difficulty in swallowing, associated with pain in the metacarpo-phalangeal joints of the right hand and the ankle and wrist joints. There was also a ganglion of the extensor tendon sheath of the index finger of the right hand.

The esophagus was dilated on April 26, 1932 and her joint symptoms have responded as usual.

Comment

From the course of this patient's arthritis, it seems reasonable to assume that improvement was the result of relieving the stricture of the esophagus. Previous to dilatation, she had regurgitated large amounts of mucopurulent, blood-streaked material from the esophagus and showed signs of having rather marked esophagitis due to retention above the stricture. Would it not be fair to draw the conclusion that the inflammatory lesions in the esophagus have acted as foci of infection which have activated the arthritis, and that drainage resulting from relief of the stenosis has permitted healing of these lesions with improvement in arthritic symptoms?

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A Study of 800 Abnormal Electrocardiograms and Associated Clinical Conditions*

By M. A. Mortensen, M.D., F.A.C.P., *Battle Creek, Michigan*

THE purpose of this communication is to emphasize the practical value of the electrocardiogram for the study of cardiovascular diseases. The tracing is based on the electrical reactions of the heart muscle during each complete cycle of action and rest. The evolution of our knowledge of the cardiogram dates back to Matteuci, who in 1843 reported the existence of reactions or currents originating in the heart muscle. The studies of Engelman, Marey, Burdon, Sanderson and Page, Gaskell, Kölliker and Mueller, and Waller, led up to the development of the string galvanometer by Einthoven in 1903. Since then there has been a rapid increase in the use of string galvanometers for research and clinical studies of the various abnormal cardiac mechanisms. The work of Wenckebach, McKenzie, Lewis, and Nicolai in Europe, and Cohn, Herrick, Smith, Wilson, Pardee, and White in this country must be mentioned as taking a leading part in the development of our present knowledge of electrocardiography.

Today the internist must realize that cardiovascular disease forms perhaps the most important group in his field to be studied and mastered. From the standpoint of morbidity and mortality it heads the list, and our program at this clinical session emphasizes this fact by devoting eighty-five periods to various phases of this group of diseases. In many diseases, such as smallpox, typhoid fever, diphtheria, scarlet fever, and tuberculosis, prophylaxis and therapeutic management have been well standardized, and as a result the physician and the laity are in a position to coöperate in the care and control of these diseases. In circulatory diseases, either acute or chronic, these phases are not so generally understood.

In the study of 800 abnormal cardiograms, we find all groups of cardiac diseases represented. They may be classified into three main groups: (1) those that are supposedly due to irritation of the myocardium; (2) the infections; (3) the degenerative processes.

Irritation of the Myocardium

In the first group we include the arrhythmias, represented by premature beats, paroxysmal tachycardia and simple tachycardia. The etiology may be toxic, directly affecting the myocardium, as occasionally seen in excessive use of tobacco, tea or coffee; or it

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may be temporarily produced by some acute infection. We must also include in this group the irritations of neurogenic origin, which occur from reflex gastro-intestinal disturbances, fear and fatigue. In this series there were thirty-seven cases with premature beats and six with paroxysmal tachycardia in which no specific evidence of cardiac disease could be discovered from history or physical findings. Focal infections were considered as possible causes but chronic follicular tonsillitis, sinusitis, dental abscesses, or acute infections, such as influenza, were not strikingly in evidence in this group of cases, and removal of some of these sources of infection was disappointing in its results. Modification of habits with reference to tea, coffee, tobacco, and elimination of intestinal disturbance and fear of serious cardiac disease, were much more productive of improvement. Premature beats were found in a considerable number of the cases belonging in the degenerative groups, but were not the main factors interfering with the well being of the patient, and apparently had little prognostic significance.

The Infections

The second group includes those having valvular lesions and associated myocarditis, usually the result of acute endocarditis with extension into the myocardium, and occasionally involving the pericardium. The great majority of these cardiac insults occurred in early life. Eighty-two cases belonged in this group, fifty males and thirty-two females, and 57 per cent of them were less than fifty years of age. The prevailing infections noted in the history were inflammatory rheumatism, chorea, acute and chronic tonsillitis, and influenza. The percentage of cases having had measles, diphtheria, scarlet fever, pneumonia and typhoid fever was not above the average found in the whole group and these diseases could not be considered of special etiological significance except in an occasional case. The lesions found were: mitral stenosis, 60; mitral regurgitation, 11; aortic regurgitation, 9; and aortic stenosis, 6. In four cases more than one valve was involved, and in three cases of mitral regurgitation there was slight suggestion of mitral stenosis, and many of those with mitral stenosis as the predominating lesion were complicated by regurgitation. Experience convinces me that the percentage of cases with pure mitral regurgitation is very small. In the 800 cases studied, 164 had systolic apical murmurs that were considered functional. The electrocardiographic findings revealed 13 with premature beats, 38 with notched P-waves, and 10 with prolonged P-R intervals. Eleven had auricular fibrillation, in most cases in conjunction with mitral stenosis, and 11 had low voltage. Poor T-waves were as follows: 31_1, 38_2, 34_3, and inverted T's, 12_1, 20_2, 27_3, all suggesting definite myocardial changes probably due to myocarditis. There were 16 cases that had arteriosclerosis in addition to the valve lesions, and we noted 16 with Q-waves larger than 25 per cent of the tallest R-wave. All of the 82 had abnormal cardiograms but those with the simpler or less extensive valve lesions revealed only minor

changes such as prolonged *P-R* intervals, notched *P*-waves, and *T*-waves of low voltage.

Degenerative Processes

The third group, comprising degenerative types, includes cardiograms of auricular fibrillation, bundle-branch block, heart block and a variety of abnormal tracings such as inverted *T*-waves, those of low voltage, and large *Q*-waves, in various combinations. We found 101 with bundle-branch block, 7 with heart block, 55 with auricular fibrillation, and 512 with myocardial degeneration with or without arterial disease in various degrees or angina pectoris. There were 511 males and 164 females in this group, and 568, or 84 per cent of these patients, were more than fifty years of age. These figures indicate a marked preponderance of the degenerative diseases in the males and confirm their occurrence in the later decades of life. In considering other etiological factors in this group, acute infections in early life seem to be of little importance. A history of influenza was obtained in 269 cases. This type of infection may aggravate an already established cardiac condition. Similarly chronic focal infections may be factors in hastening the progress of myocardial, if not of vascular, disease. The eradication of such foci seems justified.

In this group of 675 cases, the influence of heredity was shown to be of great importance, since in 72 per cent a family history of some type of cardiovascular disease was found. Among these, 111 had a positive history in both branches of the family and it is interesting to note that in these cases manifestations of cardiovascular troubles began as a rule earlier in life than where only one branch of the family was involved. These facts strongly suggest that arteriosclerosis with its degenerative processes is constitutional in nature. Obesity must also be considered as a serious factor in hastening degeneration, as it occurred in 64 per cent of these cases. The early control of this condition will be considered later in discussing management of this group.

Symptoms of Cardiac Inefficiency

The symptoms that lead to suspicion of cardiac inefficiency are rather few in the early stages of degenerative cardiovascular disease. Dyspnea is practically always the first, but is frequently overlooked by both patient and physician. The patient often considers moderate dyspnea normal or due to advancing years or over-weight. It is of the utmost importance to determine the amount of effort that produces this symptom. If it occurs during minor or ordinary activities, it should be regarded as very suggestive of cardiac inefficiency. Marked shortness of breath is not apt to be noticed by the patient unless he indulges in vigorous exercise at frequent intervals. In this group of cases dyspnea occurred in varying degrees in 558 cases, and in many was the only subjective sign of beginning cardiac inefficiency. The most difficult cases to judge from the point of history and symptoms were those of very sedentary habits, and here a few vigorous hops or climbing a flight of stairs were usually a convincing proof of a limited cardiac efficiency.

Palpitation or heart-consciousness is perhaps the next most frequent symptom experienced in this group. It is essential to obtain a clear idea of what the patient may mean by palpitation, as it may be a simple tachycardia not related to effort. Palpitation was noted 322 times. When these two subjective symptoms, dyspnea and palpitation, appear together with arterial hypertension and obesity, we should not fail to make a thorough study of cardiovascular efficiency.

Chest pain or precordial discomfort is another important symptom; it does not always mean angina pectoris but may mean aortitis or some other form of heart disease. This symptom occurred 296 times but was radiating in type in only 140 cases and not all of the latter justified the diagnosis of angina pectoris.

Our examination included search for such objective findings as basal pulmonary congestion, abnormal heart sounds, blood pressure, cardiac hypertrophy, and cardiographic findings. Basal congestion was noted 166 times and is worthy of careful study from day to day as evidence of the patient's progress in overcoming decompensation. High blood pressure findings are of extreme importance as they give a picture of cardiac labor with the patient at rest and must be recognized as a handicap to the heart muscle. The systolic pressure was found to be above 150 in 415 cases, and below in 260; the diastolic was above 90 in 366, and below in 309 cases, showing a decided preponderance of blood pressures above 150/90 mm. Hg. In this group a larger percentage of those with blood pressure less than 150/90 occurred in the cases having bundle-branch block, auricular fibrillation, and in a group classified as simple chronic myocardial degeneration. Among these are many with arteriosclerosis, diagnosed as such, not by blood pressure, but by the presence of tortuous or palpable arteries and increased density of the aorta or peripheral vessels determined by X-ray. It was found important to make X-ray examinations of the arteries in the lower extremities in diabetes in order to anticipate possible gangrene, and in other cases to verify the probability of intermittent claudication, as these conditions are often found with a blood pressure less than 150/90. As the diastolic pressure progresses above 100, the prognosis for cardiac efficiency and length of life becomes increasingly unfavorable. In the study of blood pressure, whether high or comparatively low, it is very necessary to consider pulse pressure, which is of important significance in cardiac efficiency.

Heart murmurs are of less significance in this group. Only 49 were found which could be considered organic with reasonable certainty, as compared to 180 murmurs which were thought to be functional. All of these latter were systolic in time and nearly all were located at the apex. These functional murmurs are often diagnostic pitfalls and sources of anxiety to physician and patient respectively. To determine the true significance of murmurs is important, but of equal if not greater importance in this group of cases is a careful study of the heart tones, whether muffled, distant, or distinct, or of good quality. The term "heart tones" is not limited to the valve

sounds alone but includes the muscle tone, the result of the ventricular contractions. Tones that were poor in quality, or muffled, occurred in 324 cases in both the reclining and upright positions and aroused suspicion as to the quality of the heart muscle or the possibility of pericardial effusion. Gallop rhythm, which was found in 34 patients, occurred only in the more serious cases, and should always be regarded as an unfavorable prognostic sign.

In this group of cases of degenerative cardiovascular disease the cardiogram is of great value in forming an opinion of the condition of the myocardium. We found extra systoles 69 times, notched *P*-waves 16 times, prolonged *P-R* interval 44 times, all of which are of interest but not of great significance. Other findings deserve a little more detailed consideration.

Auricular fibrillation occurred 67 times and in this group must be considered indicative of myocardial degeneration. It often has a fair prognosis under proper therapeutic management. Bundle-branch block occurred 101 times and whenever found should be considered as positive evidence of extensive myocardial degeneration. In this series, where it was possible to follow up our cases, 55 per cent died within fifteen months after the bundle-branch block was discovered. Among these cases of bundle-branch block a few are found which present no symptoms either subjective or objective except the cardiogram, and these may go on for years without any symptoms of cardiac inefficiency; but in spite of this each case deserves careful management and the patient should be warned against unusual effort. Muffled heart sounds are very frequently found to be accompanied by dyspnea, precordial discomfort, poor tolerance for exercise, moderately high blood pressure or evidence of a limited cardiac efficiency, and these cases should be managed with extreme care. The cases showing low voltage numbered 134, and in some of them repeated observations are deserving of special interest. A number of such cases has gradually developed impairment of cardiac efficiency and as a group they deserve a careful study with repeated observations to determine the prognostic value of this type of tracing.

The Significance of Some Abnormal Cardiograms

The inverted *T*-wave deserves mention, being found with considerable frequency in the degenerative cases. It occurred 231 times in T_1, 172 times in T_2, and 186 times in T_3. Inverted T_1 and T_2 alone or in combination are considered of pathological significance, but inverted T_3 alone is not looked upon as evidence of disease. I am not sure that inverted T_3 is without significance, especially if T_2 is of low voltage. I am inclined to believe that a low T_2 with inverted T_3 will often develop into an inverted T_2 and T_3 and thus may be of pathological significance. In 11 cases where cardiograms have been taken at intervals over a period of years, I have found this change to occur, coupled with evidences of progressive cardiac inefficiency.

The *T*-waves of low voltage are of more frequent occurrence than the inverted *T*-waves, but in similar pro-

portions, there being 234 T_1, 205 T_2, and 207 T_3 of low voltage. Both the inverted T-waves and those of low voltage occur with greatest frequency in patients with general arteriosclerosis and obesity, and must be looked upon as positive evidence of myocardial degeneration. We find that not a few of the poor T-waves later become inverted. I have noted these changes in 15 cases. These observations are dwelt on in detail to emphasize the importance of low voltage T-waves as evidence of insidious changes taking place in the myocardium. They deserve our careful consideration when interpreting the cardiogram, and attention should be called to T-waves as being suggestive of low voltage before they reach the point of measuring 1 mm. or less.

Large Q-waves in Lead III of more than 25 per cent the height of the R-waves have been brought to our attention by Pardee as evidence of pathological lesions of the left ventricle. In our series, large Q-waves were found 257 times and occurred with greatest frequency in cases of angina and general arteriosclerosis. In 137 cases of angina, a large Q-wave was found 95 times. Here again I suggest the presence of an inverted T_3 and large Q-wave as still more positive evidence of myocardial disease as far as Lead III is concerned. Further study of the poor T and inverted T and large Q-waves should be encouraged and, where possible, the nature of pathological lesions of the myocardium determined.

The coronary or cove wave in coronary thrombosis is another abnormal picture that is of diagnostic value confirmatory of the subjective or objective findings of this serious cardiac condition. In my experience, the cove, or abnormal S-T interval, appears within a few days after the insult, and in the cases that survive and finally develop a fair myocardial efficiency, the tracing returns to approximately normal as far as the S-T interval is concerned. The nearer the tracing approaches to normal, the better the prognosis. Cases under observation for from three to seven years have tracings with little or no evidence of the coronary wave. This wave was found 26 times and occurred in cases of coronary thrombosis or angina pectoris only. In one case attacks of paroxysmal tachycardia occurred during a stormy convalescence. Here, absolute rest, small doses of quinidine sulfate and digitalis and proper use of sedatives, proved most effective in eliminating the attacks.

Comment

The management of the various types of cases found in this review may be briefly outlined. The premature beats and paroxysmal tachycardia are of minor importance but sometimes are very annoying to the patient. The best program in my experience is to eliminate anxiety or fear and consider focal infections and toxins, such as coffee, tea and tobacco, as possible causes. It is also important to eliminate reflex disturbances of gastrointestinal origin. In addition we should consider the advisability of the use of quinidine sulfate and sometimes of a mild sedative for relief. Auricular fibrillation, another form of arrhythmia, deserves a good prognosis under proper management. Careful judgment

must be used in the exhibition of quinidine sulfate, as permanent relief of arrhythmia results in only a small percentage of cases. It should be avoided in severe cases of mitral stenosis for fear of unpleasant complications. Wherever there is a suggestion of decompensation, digitalis is the remedy of choice. For the cases with arteriosclerosis and hypertension, bundle-branch block, and associated myocardial degeneration, it is very important to recognize myocardial changes as early as possible and take into consideration the effect of arterial hypertension, the condition of the pulse pressure and the presence of obesity.

In developing a program for these cases it is of great value to outline a proper amount of exercise, as experience proves that it is of extreme importance to maintain the best possible muscle tone and endurance in these individuals. Each case must be considered individually when developing a program of exercise. A careful weight reduction for the obese is of great importance. With patients under close observation, a rather vigorous program of weight reduction by diet and physiotherapy (hydrotherapy, heliotherapy, and massage) may be ventured in the more robust types, if definite evidence of myocardial inefficiency is lacking. In such cases a loss of five to eight pounds a week may be risked, but with cases not under close observation, a loss of one or two pounds a week is usually safer. The control of food intake and exercise is of greatest importance in these cases. It is surprising how little food is necessary to maintain the desired weight when it is once established. In cases of marked hypertension, particularly those with high diastolic pressure and marked renal inefficiency, the protein intake can be safely reduced to 50 or 60 grams a day, or lower, over a considerable period of time. The use of fruits and fruit juices should always be encouraged and should furnish a considerable portion of the carbohydrate.

Experience convinces me that the greatest reduction in blood pressure and improvement in cardiac efficiency is obtained by reduction in weight, exercise, and a careful regulation of the individual's daily program with reference to work and recreation. Nervous tension, anxiety and fear, should be combatted in all of these cases. Institutional management affording careful observation over considerable periods of time, with the various forms of physiotherapy, dietetic regime and personal contact with the patient, usually produces the best results.

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The Value of the Posterior-Anterior Chest Lead in Cardiac Diagnosis*†

By Abraham Lieberson, M.D., and Frank Liberson, M.D., *New York*

FROM the very nature of the cardiac action current, it is evident that the number of leads which can be used to conduct the current from selected skin zones to the string galvanometer is legion. It was inevitable that in cases where the three conventional leads failed to furnish enough information about the condition of the heart muscle, some other one, taken in another plane, would be tried in the hope that it might supply the needed data. Thus Waller[1] (1887) placed his electrodes all over the body, and in all the natural orifices, searching for "significant" leads. Lewis[2] (1909), studying the action of the auricles in fibrillation, discovered that the workings of this chamber could be best investigated by a special additional lead from the front to the back of the chest. To date this has found very little clinical application. Recently, however, Wolferth and Wood[3] (1932) have applied the chest lead (from front to back of chest) in the diagnosis of coronary occlusion. They report one case where the three conventional leads were practically normal, except on the fourth day, whereas for eight days after the original infarction the Anterior-Posterior chest lead showed striking deviation of the *S-T* interval; and another instance where the evidence for coronary occlusion was present in only two leads, the first and A-P chest leads, the *S-T* deviation being much more striking in the A-P chest lead than in the first lead. They examined 33 non-coronary cases as controls and found no deviation of the *S-T* interval in the A-P chest lead in these cases.

Using a slightly different technic (smaller electrodes and a Posterior-Anterior direction, to be detailed later), and taking the chest lead in conjunction with the usual three in a series of 75 cases, 20 of which were normals, 50 cardiac suspects, and 5 "coronaries", we likewise found the additional chest lead very useful in determining the presence and extent of coronary involvement. We report the following case as especially demonstrative of the fact that the chest lead may point to a diagnosis of coronary occlusion where neither the clinical picture nor the E.K.G. taken with the usual leads suggests it. Often the conventional leads begin to show at a later date those changes seen days and weeks before by the chest lead.

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†From the Beth Israel Hospital, N. Y., and the U.S.P.H. Service Hospital, Stapleton, S. I. By permission of the Surgeon General, U.S.P.H.S.

CASE REPORT

H.M., white male, age 53, admitted to the U.S.P.H.S. Hospital, Stapleton, S.I., December 1, 1931. The past history was negative, except for moderate occipital headache and nocturia for ten years. On November 27, 1931 the patient's left leg suddenly felt weak, and by the 30th it was limp and helpless. He entered with this sole complaint of weakness of the left leg.

Physical Examination. A well-developed white male of 53, not acutely ill. Head, heart, lungs, and abdomen negative. The left foot showed flaccid paralysis. The blood and

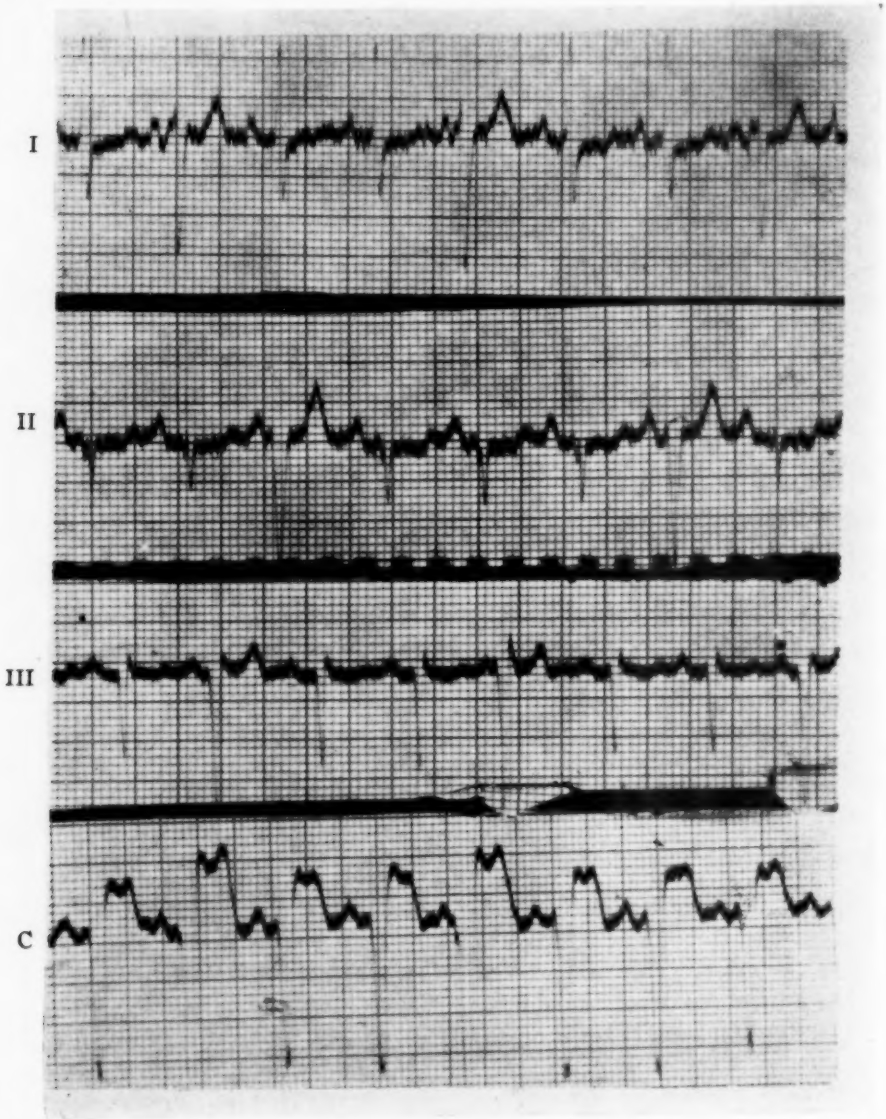

FIG. 1. (January 25, 1932). Patient showed no cardiac signs (except fall of blood pressure from 170 to 120 mm. Hg in three weeks). Leads I, II, and III are considered as showing no definite myocardial damage, although there is a suggestion of a slightly high *T* take-off in Lead III. The Posterior-Anterior chest lead shows, however, an *S-T* elevation of fully 5 millimeters—practically pathognomonic of coronary occlusion.

spinal Wassermann, urine and blood count were all negative. Temperature 37°; pulse 90; respiration 20; blood pressure 170/90 mm. Hg. The headaches and hypertension suggested a cerebral thrombosis or hemorrhage as possible cause of this monoplegia. Aside from the hypertension the case appeared to be of neurological interest only. The patient did well under rest in bed and physiotherapy to the affected leg, complaining only occasionally of pain in the head or "an upset stomach". His blood pressure, however, fell from 170/90 mm. Hg to 120/66 mm. Hg, and it was thought advisable to make an electrocardiographic examination before transferring him to the Neurological Service. The graph obtained, January 25, 1932, using the three conventional leads and the Posterior-Anterior chest lead was surprising to the clinician (figure 1). The three usual leads showed every fourth beat to be ectopic; there was L.A.D. (old nomenclature). Aside from an occasional, questionable high take-off of the *T*-wave there was in these leads no definite indication of myocardial damage. In the P-A chest lead, however, instead of a symmetrical *T*-wave arising from the isoelectric point, there was fully 5 mm. elevation of the *S-T* interval, with total asymmetry of the *T*-wave. In spite of the negative evidence in the three conventional leads, and the absence of clinical symptoms, it was postulated that the patient had definite coronary damage, the type of curve suggesting an acute process.

The patient was transferred one day later (January 26, 1932) to the Neurological Service of the U.S.P.H.S. Hospital, Ellis Island, where his pulse was found to be very irregular and intermittent, varying between 62 and 104 during the next two days. This was thought to be due to the excitement incident to his transfer. A teleoroentgenogram taken at this time showed a contour of the heart suggesting slight enlargement to the left, but on the whole probably within normal limits in size and shape. There was slightly increased density in both bases and faint triangulation of the cardiac shadow suggestive of myocardial weakness. The E.K.G. of this date (January 26, 1932) employing only the three conventional leads was reported as showing frequent ventricular extrasystoles, L.A.D., but no significant myocardial changes. After two days the patient began to feel better. The use of the left leg slowly returned in part, and he was discharged improved February 1, 1932.

Patient was readmitted to U.S.P.H.S. Hospital, Stapleton, S.I., on February 9, 1932 as an urgent case, complaining of pain in the upper abdomen and chest of four days' duration, beginning after a heavy meal, and accompanied by a mild non-productive cough and difficulty in breathing.

Physical Examination. Patient acutely ill; facies anxious, shallow and rapid breathing, moderately coarse râles at both bases with altered breath and voice sounds, especially on the right. The apex beat was in the fifth interspace, 8 cm. to left of the midline, and in the midclavicular line. Rhythm regular, pulse weak and thready. The temperature was 38° on admission and varied between 36.4° and 37.8° for the next five days. There were 14,400 W.B.C. with 74 per cent polymorphonuclears. Bedside X-ray at this time showed enlargement of the cardiac outline, with pulmonary congestion but no evidence of pneumonia. The patient for the first two days was in such a state of shock that the clinician thought it inadvisable to subject him to even the slight strain of electrocardiographic examination. He was given small doses of digitalis (2 grains a day) and showed improvement. On the fourth day (February 12, 1932) the E.K.G. (figure 2) showed a definite intraventricular block and a faint suggestion of an elevated *S-T* interval in the conventional leads. The P-A chest lead showed complete inversion of the *T*-wave, a very unusual finding in this lead. The complexes in the chest lead had changed so in the short period between January 25 and February 12, that one had to consider them as evidence of an active process taking place in the coronaries. An E.K.G. taken three days later, February 15, 1932 (figure 3) pointed again to coronary involvement, and showed for the first time a definitely elevated *S-T* segment in both Leads II and III; the P-A chest lead showed again marked changes in the low voltage *T*-wave.

With the rapid change in the complexes over the three week period, and finally with

the almost pathognomonic E.K.G. in all leads at the end of this period, the diagnosis of coronary occlusion could be made with definiteness, and was apparently corroborated by the later clinical course. At 2:30 the next afternoon, February 16, 1932, the patient suddenly developed a convulsive attack with stertorous breathing which rapidly changed to a Cheyne-Stokes type. The heart stopped; the breathing ceased soon after. In spite of medication he died within fifteen minutes. The mode of death appeared very much like that seen in ventricular fibrillation.

Comment

From the electrocardiographic point of view the interesting fact in this case is that by use of the P-A chest lead coronary occlusion could be diagnosed with some definiteness at a time when no other evidence for it (except

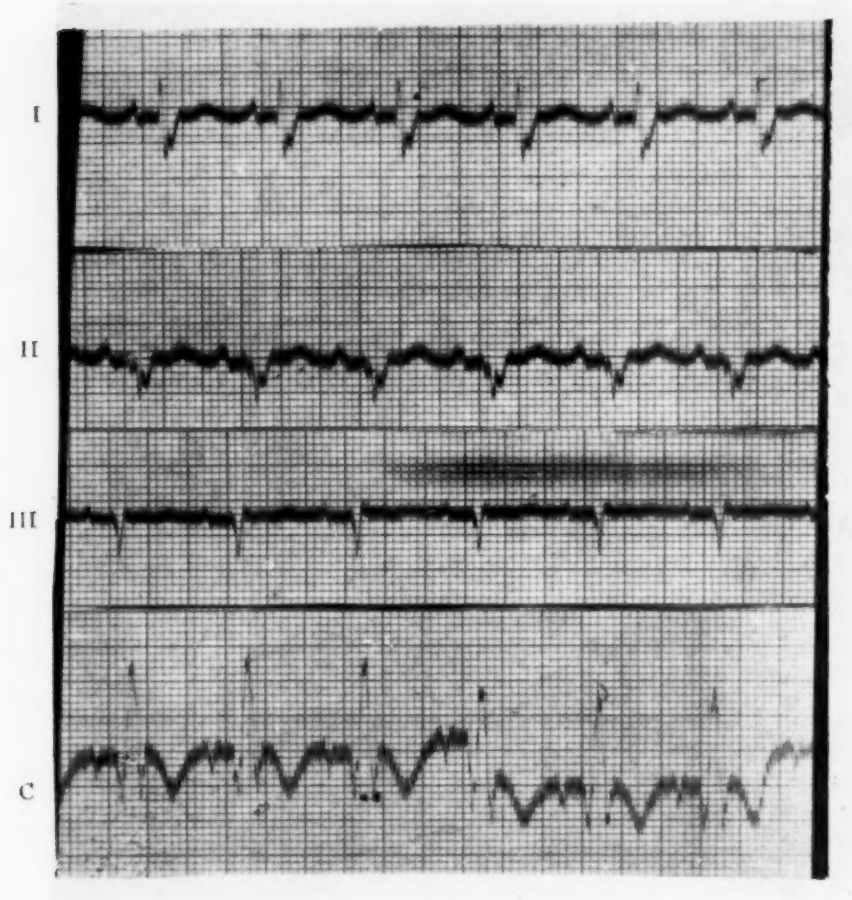

Fig. 2. (February 12, 1932). One week after an attack of pain in the epigastrium and chest, followed by leukocytosis (14,400) and a temperature of 37°-38°C. Leads I, II, and III show intraventricular block, but no definite change in the *S-T* interval, while the Posterior-Anterior chest lead shows marked inversion of the *T*-wave—an extremely rare occurrence in this lead. The fact that this graph differs so from the former one would indicate that we are dealing with an acute process—coronary occlusion.

perhaps falling blood pressure) was present. The early findings in the conventional leads were quite insufficient to warrant such a diagnosis. When carpossible to demonstrate in all leads an *S-T* interval abnormal enough to definitely indicate coronary occlusion. When this occlusion took place is hard

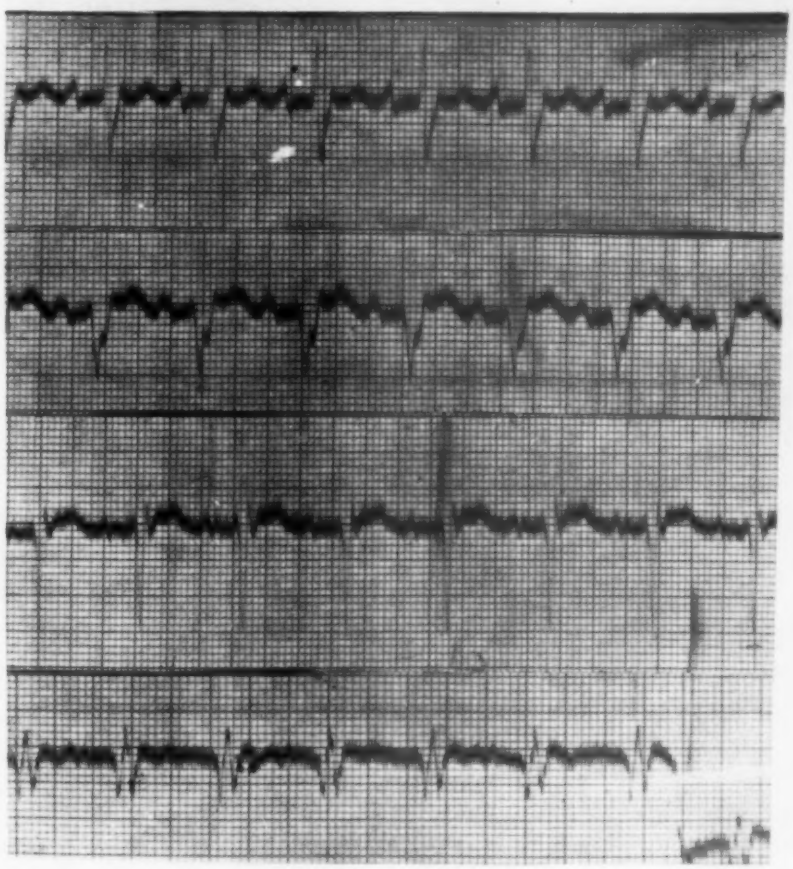

FIG. 3. (February 15, 1932). Taken three days after figure 2. There is a definite elevation of the *S-T* segment in Leads II and III. The conventional leads have assumed the typical aspect of recent coronary infarction. The Posterior-Anterior chest lead also shows marked changes from the previous tracing.

diac symptoms appeared, the P-A chest lead showed clearly those manifold rapid changes in the ventricular complexes that are so suggestive of coronary occlusion. It was not until the day before death, however, that it was to say from either the history or the tracings, but in the first E.K.G. (January 25, 1932) there is already definite evidence (in the P-A chest lead) of coronary occlusion (possibly a slow closure); while the sudden attack of

epigastric pain and beginning decompensation of February 5, with the subsequent electrocardiographic evidence of acute coronary closure in the conventional leads, is especially suggestive of a recent thrombosis.

ter), the "Right Arm" electrode being placed along the medial edge of the spine of the right scapula (about the level of the third dorsal spine), the "Left Arm" electrode going to the cardiac apex area. Great care is taken to avoid undue resistance by keeping the saline solutions warm, cleansing the skin thoroughly, and rubbing it lightly with a very fine copper wire

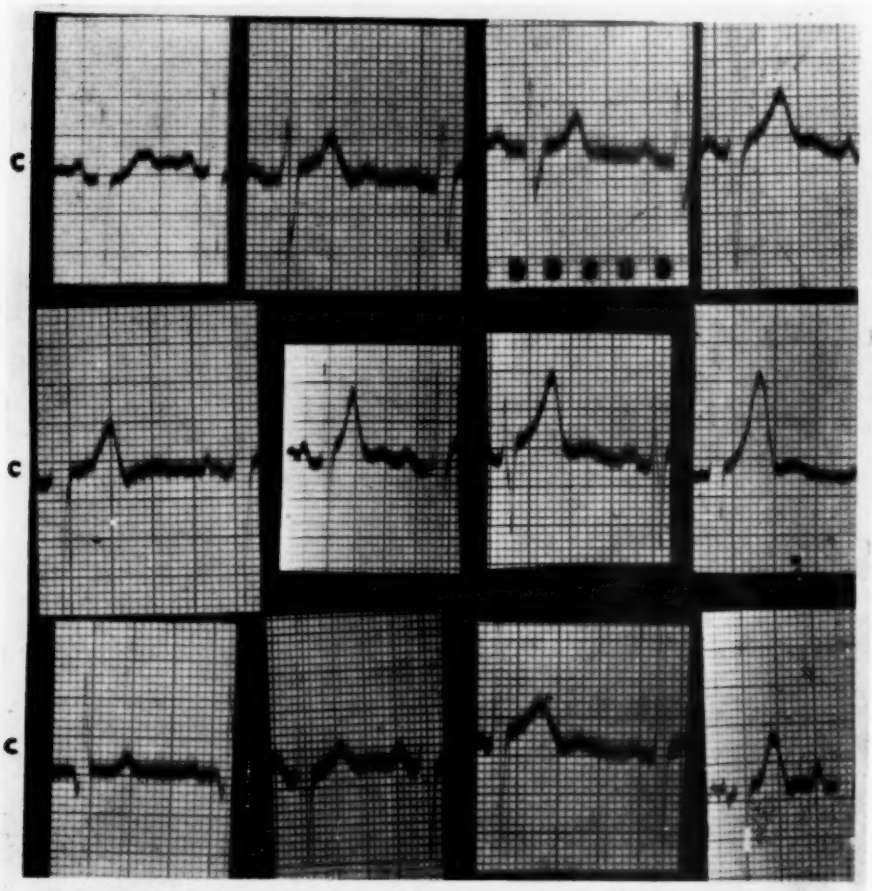

FIG. 4. Several examples of normal findings in the Posterior-Anterior chest lead, either in normal individuals, or in cardiacs showing normal electrocardiograms. Note that *P* is upright; *Q-R-S* diphasic and relatively large; the u-waves are prominent. The *T* take-off is never elevated more than 3 millimeters. Perhaps most important is the symmetry of the *T*-wave.

The technic used in obtaining the chest leads consists of the application of small, wet, gauze-covered copper electrodes (about one inch in diame-

brush before applying the burnished electrodes. The string is carefully standardized before the taking of each lead; and no tracing is considered satisfactory that shows appreciable overshooting.

Thus far the electrocardiograms of 75 individuals have been taken, showing all four leads. Of these, 55 were cardiac suspects (5 of whom were cases of coronary damage) and 20 were normals. By a study of these normals it was found that the Posterior-Anterior chest lead is not less constant than the conventional leads. It shows characteristically a small upright *P*-wave; a biphasic *Q-R-S* of high amplitude; a relatively large, upright, symmetrical *T*-wave; and an *S-T* take-off of no more than 3 mm. elevation above the isoelectric line. The u-waves are usually prominent. A number of typical tracings of the Posterior-Anterior chest lead are shown in figure 4, and indicate the usual range of variation in this lead. An asymmetrical or inverted *T*-wave is always abnormal. The most constant finding in an acute coronary closure is a high *S-T* take-off with resultant asymmetry of the *T*-wave. This finding in the Posterior-Anterior chest lead may precede similar changes in the other leads by days or weeks. This would tend to indicate that the axis of this chest lead is so situated as to register more surely the lesions produced by cardiac infarction. We believe, therefore, that the Posterior-Anterior chest lead is of definite clinical value.

Conclusions

A case is presented where marked *S-T* interval elevation was seen in the Posterior-Anterior chest lead fully three weeks before similar changes in the conventional leads. This permitted the diagnosis of coronary occlusion in the absence of any other definite sign. The further course of the illness and the later electrocardiograms appear to have substantiated this diagnosis.

Twenty normal individuals were studied to determine the normal range of variation in the Posterior-Anterior chest lead. This information helped substantially in the diagnosis of coronary involvement, which was made in five out of fifty-five cardiacs examined.

We wish to express our indebtedness to Medical Director M. H. Foster, in charge of the U.S.P.H.S. Hospital, Stapleton, S.I., for the privilege of using the hospital records, and to Assistant Surgeon S. P. Cooper, in charge of the Medical Service, for his kind coöperation in obtaining the electrocardiograms.

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Localized Atrophy of Subcutaneous Fat Following Repeated Injections of Insulin*†

Report of a Case

By Friedrich Engelbach, M.D., *Ann Arbor, Michigan*

THE localized atrophy of subcutaneous fat following repeated injections of insulin was first described by Depisch[1] in 1926, and since then has been reported by Barborka,[2] Davison,[3] Mentzer and DuBray,[4] Carmichal and Graham,[5] Chapman,[6] Rabinowitch,[7,11] Lawrence,[8] Priesel and Wagner,[9,17] Avery,[10] Fischer,[12] McCormick and Moorhead,[13] Stransky,[14] Price,[16] Boller,[18] Eeg-Olofsson,[19] and Williams.[21] Less than sixty cases are recorded in the literature, and of these, less than half are described even briefly, and only two biopsy reports are given.

The atrophy noted was almost always at sites of frequent insulin injections and began several months to several years after starting the injections of insulin into the areas later affected. It always involved the subcutaneous fat but produced no apparent changes in the skin or in the underlying muscles. The condition was more common in females than in males, and apparently was not related to the age of the patient, the duration of the diabetes nor to its severity, nor to the make or amount of insulin used, nor to the methods used in sterilizing syringes and needles. Fischer[12] found the condition present in two-thirds of a group of diabetic children taking insulin. Depisch[15] states that about 10 per cent of patients taking insulin have localized atrophy of subcutaneous tissues at the sites of injection. In one case described by Priesel and Wagner,[17] the fatty atrophy was apparent only after the boy began to gain weight, there being no deposits of fat in the areas frequently used for the injection of insulin. Chapman[6] reported a patient in whom fat returned in the areas of atrophy, these areas appearing normal two and a half years after discontinuance of the use of insulin. Various other authors report partial return of the fat. Boller[18] and Stransky[14] report a case where the atrophy of fat was noted at the areas of repeated insulin injections and also in one cheek where no injections had been made. The fatty atrophy of the cheek was treated by weekly procaine injections into the area, and three and a half months later the cheek appeared almost normal. Some of the patients experienced pain on the injection of insulin, but many did not. Boller be-

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†From the Department of Internal Medicine, University of Michigan, Ann Arbor.

lieves that if procaine is injected with the insulin no pain will occur and no fatty atrophy will result from its use.

Various theories have been advanced to explain the disappearance of the subcutaneous fat. Rabinowitch[7] was unable to demonstrate the presence of lipase in insulin as a possible cause. Priesel and Wagner[9] believe that the tricresol used in preserving insulin is the cause, but Depisch[15] gave daily injections of tricresol solution for over two months without producing a fatty atrophy. Avery[10] believes the subcutaneous fat atrophy is a nonspecific reaction, the result of repeated small traumata to the panniculus adiposum. Fischer[12] considers the most plausible explanation to be a low grade inflammatory process set up by repeated injections of insulin, the resultant damage causing replacement of the soft areolar tissue by scar tissue. He also considers the possibility that insulin may raise the level of local tissue metabolism, and thus eventually lead to the disappearance of fat by oxidation. Depisch[15] believes that insulin causes injury to the nerve fibers. Williams[21] thinks that insulin may injure the membrane that covers the fat cells, releasing fat globules, which, acting as foreign bodies, result in the formation of histiocytes which take on lipophagic activity.

Mentzer and DuBray[4] report that sections from biopsy of the lesion show no lymphocytic foci and no evidence indicative of inflammatory changes. Eeg-Olofsson[19] on microscopic examination found most of the change to be due to an ordinary atrophy of fat tissue, but that occasionally small areas of round cell infiltration were found around the vessels. He found nothing which threw light on the origin of this atrophy of the fat tissue.

Case Report

Patient M.B., thirty-two year old American woman, was first admitted to the University Hospital March 20, 1929, at which time she complained of weakness and dizziness of two months' duration and a loss of twenty pounds during this period. Physical examination showed evidence of some recent loss of weight, mild neuroretinitis, a slight diffuse enlargement of the thyroid, and a barely palpable liver and spleen. Urine showed 4 plus sugar and 2 plus diacetic acid. A diagnosis of diabetes mellitus was made and she was placed on a diet of 55 gm. protein, 220 gm. fat and 65 gm. carbohydrate with insulin as needed, the dosage varying from eight to seventy units daily. She was advised to continue the diet and insulin after discharge. On April 21, 1932 she was brought into the University Hospital in diabetic coma, having taken more food than her diet allowed and not having controlled with insulin her glycosuria of several months' duration. She was given large doses of insulin, recovered from the coma, and after a stay of about two weeks' duration was discharged on a diet similar to that prescribed before, with fifteen units of insulin twice daily.

In March 1931, about two years after starting to use insulin, she noticed disappearance of the subcutaneous fat in the anterior and lateral aspects of the upper arms, which were the areas where the insulin had been injected. In March 1931 she stopped using the arms as sites of injection and began using the anterior parts of the thighs. About six months later fatty atrophy began to occur in the anterior parts of the thighs and has been progressive since then. During the last year the fatty atrophy of the left arm has tended to diminish slightly. The accompanying photographs illustrate the extent of the fatty atrophy. In the depressed areas muscle could be felt beneath the skin, there being no evidence of fat at these points. Sensation was entirely normal and there was

FIG. 1

no loss of muscle power. No pain had been experienced from the injections of the insulin which had been made repeatedly in the same areas.

Biopsy was done, a piece of skin and subcutaneous tissue being removed from the affected area on the anterior part of the right thigh. This was examined in the pathology laboratories of the University Hospital, and Dr. Carl V. Weller has been kind enough to furnish the following report: "The pathological changes resulting in the local atrophy in this material are confined to the panniculus. In the involved lobules the adipose tissue cells are very small and collapsed with a marked reduction in the total lipid content. With this change there is an increased number of small blood vessels, some with slight thickening of the walls, and there is a slight perivascular lymphocytic infiltration. Some of the involved fat cells contain a small amount of albuminous material, but there is no evidence of fatty acid crystals or of soap formation."

FIG. 2

SUMMARY

A case of localized atrophy of the subcutaneous fat following repeated injections of insulin has been described.

Although the actual mechanism that causes the disappearance of the subcutaneous fat is not known, the condition seems to be associated with

frequent injections in localized areas, and, to prevent the condition it would be advisable to scatter the doses of insulin over as large an area of the body as possible.

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Primary Spondylitis*†

By W. Paul Holbrook, M.D., F.A.C.P., Robert M. Stecher, M.D., and Edward M. Hayden, M.D., *Tucson, Arizona*

IN approaching the study of spondylitis, or arthritis of the spine, one may properly ask that its relation to the large group of chronic arthritide be defined.

Any discussion of chronic arthritis is at present most confusing because of the numerous classifications and the many variations in terminology. Classifications now in use are, in general, based upon etiological or pathological suppositions. Etiological classifications can be of little help, as no single factor has definitely been proved to be the specific causative agent. One needs to recall but a few of the present affirmed etiological factors to realize that chronic arthritis is as yet a disease of unknown origin. The neurogenic theory, the theories of vascular deficiency, trauma, endocrine deficiency, presenile changes, disturbed metabolism, infection, and many other hypotheses all have ardent supporters. Pathological groupings are but little better as material is very difficult to secure at progressive stages, and scattered observations during different stages of the same disease are apt to be misleading. The number of pathological examinations that have been correlated with clinical studies are far too few upon which to base an opinion. One of us (W.P.H.) has asked many pathologists in this country and abroad for such information only to be told that the pathologist's interest lay elsewhere, or that insufficient material could be secured to be of any value.

It has been a hopeless task from our standpoint to fit our arthritis patients into existing ready-made groups. During several recent medical conferences in which arthritis was a special interest, leading authorities have proposed more than a dozen separate classifications and have recommended equally diversified treatment. Because of this existing confusion and the absence of uniform clinical concepts, we decided to study a large group of arthritics completely and uniformly. These studies were made under the most complete control and supervision of the patient and in ideal climatic surroundings. During the past eighteen months three hundred patients with chronic arthritis have been selected from our hospital and outpatient department for this study. We have tried to consider these patients from two standpoints. We have attacked the problem as a research which involved many exhaustive tests and examinations. But we have also attempted the simplest clin-

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†The Desert Sanatorium and Institute of Research, Tucson, Arizona.

ical approach, and it is this practical clinical study that is responsible for the grouping shown in table 1.

The average length of time these patients were under observation was slightly over five months. Many of them were in the hospital the entire time, and nearly all of them were hospitalized at intervals. This group of patients has been carefully analyzed as to history, physical examination, laboratory, roentgenologic studies, and response to treatment. We have not assumed any specific etiology but have grouped them solely upon a clinical basis.

The greater portion of our patients come from widely separated points geographically, and so should represent an accurate cross-section of types. It is only fair to say that most of them are "last-resorters", and so should be thought of as representing the very chronic or advanced stage of the disease.

It seemed at the beginning an endless task, but there have emerged to date six well defined groups. No argument is being made at this time for a separate etiology. Indeed it is wholly possible that several groups may have one or many etiological factors in common. We have, however, found such a grouping practical and very helpful in selecting therapeutic measures; table 1 presents a brief analysis of the six groups.

Group I is an afebrile, insidious, progressive, symmetrical, deforming, and crippling disease. Arthritis deformans, rheumatoid arthritis, atrophic arthritis, and proliferative arthritis are other common terms loosely applied to any severe polyarthritis. This group is separated from Group II, which appears infectious in its manifestations, because of Group I's marked predilection for women beyond the third decade, its symmetry, the lack of fever, the marked and wide-spread demineralization, the early cartilage destruction, the trophic skin and muscle changes, and the complete failure of therapy when directed toward infection or when the problem is attacked solely from the standpoint of foci of infection. It is a disease often dramatically affected by the patient's emotional life, and in most instances is associated with some form of gastrointestinal dysfunction. If infection plays a major rôle in this group of cases, its manifestations are not obvious, and there are surely other necessary factors.

Group II Arthritis is most commonly termed chronic infectious. It is also known as atrophic, or rheumatoid, and is referred to in many other terms. It is in general not separated from Group I. In contrast to Group I, however, there is fever, malaise, and other constitutional symptoms of infection. Everyone is familiar with this picture of infectious polyarthritis with pain, heat, redness, and swelling in the joints at some stage of the disease and usually at the onset. In this most acute phase it is with difficulty that it is differentiated from acute rheumatic fever.

Group III Arthritis is often classified as osteoarthritis, hypertrophic arthritis, degenerative arthritis, and streptococcus viridans arthritis. This is a disease which comes on rather late in life with insidious onset, and usually first noted because of stiffness of the spine or fingers. Heberden's nodes

TABLE I
CLINICAL GROUPING

	I	II	III	IV		V	VI
				SPONDYLITIS			
				(A)	(B)		
Sex	5F-1M	2M-1F	5M-1F	M Only	M Only	1F-1M	2M-1F
Age Onset	30-50	Any Time	Late	20-30	20-40	40+	Any
Pos. Hist. Before Onset	Psychic Constip.	Head Infection	None	Fatigue Constip.	Severe Infection	None	Infection
Onset Ac. or Insid.	Insid.	Acute	Insid.	Insid.	Either	Insid.	Acute
First Joint	Prox. Phalang.	Any	Spine Fingers	Spine	Spine	Wt. Bearing	
Joints Invol.	Peri.	Peri.	Any	Spine	Spine		
Joints P.H.R.S.	P.-S.	P.-H.-R.-S.	P. and S.	P.-	P.-	P.-S.	P.-
Deformity	Yes-Char.	Not Char.	No	Yes-Char.	Yes	Occ.	No
Symmetrical	Yes	No	No	Yes	Yes	No	No
Trophic Skin and Muscle	Yes	Not Early	No	No	No	No	No
Wt., Gen. Health	Good	Reduced	Good	Reduced	Reduced	Good	Good
Const. Type	3 or 4	Any	1 or 2	3 or 4	Any	1 or 2	Any
B. P.	Low	Any	Up	Low	Any	No-Up	Normal
Heart Lesion	No	Often	No	No	No	No	No
Foci	No	Yes	Not Marked	Not Marked	Not Marked	No	Yes?
Other Pos. Findings	Seldom Any	Often Many	Seldom Any	Seldom Any	Many	Over-weight	
Fever-Onset-Course	No-Low	Yes	No	No	Occ.	No	No
Treatment	Diet Exercise	Foci Vaccine	General	Diet Posture	Foci General	Reduce Posture	Foci General
LAB. RBC & HB	Normal	Anemia	Normal	Sl. Anemia	Normal	Normal	Normal
LAB. WBC-Diff.	Normal	High	Normal	Normal	Up-Normal	Normal	Normal
LAB. Sedimentation	Rapid	Rapid	Normal	Rapid	Increased	Normal	?
LAB. Gastric HCl	Low-Absent	Normal	Normal	Low-Absent	Normal	Normal	Normal
LAB. BMR	Normal	Normal	Normal	Normal	Normal	Low	Normal
X-RAY Periartic.	Yes	Yes	No	No	No	No	Yes?
X-RAY Cartilage	Yes-Early	Yes-Late	No	No	No	Yes	No
X-RAY Bone	No	Yes-Late	Yes	No	Yes	No	No
X-RAY Demineral.	Yes-Early	Not Early	No	No	No	No	No
G.I. Tract	Colon	Sigmoid	Normal	Colon	Sigmoid	Normal	Normal

often occur, and there is usually only pain and swelling of the joints without heat or redness. The weight and health are excellent. The blood pressure is normal or elevated, and the constitutional type tends toward the sthenic. It is relatively a benign disease producing lipping and spurring in various joints.

Group IV is the group of primary spondylitis which we will discuss shortly.

Group V is often referred to as metabolic, traumatic, or menopausal. The important factor in this group is that a weight-bearing joint, usually a hip or a knee, is involved. Ordinarily, not more than one or two joints are affected, and this is one respect in which it differs from Group III osteoarthritis which is a generalized disease. Patients of Group V are usually overweight with no significant findings except in the weight-bearing joints or in joints that have suffered trauma. The riding master with an arthritis of the hips, the watch-maker with involvement of the cervical vertebrae, and the trap-shooter with arthritis of the shoulder are included as well as the overweight, middle-aged woman with painful knees.

Group VI may properly be termed pre-arthritic and in it are included all manifestations of neuritis, myositis, bursitis, and fibrositis.

We have included spondylitis for purposes of simplicity in grouping as one of the groups of chronic arthritis. Primary chronic arthritis of the spine represented by Group IV may be separated into two general groups: Type A (without bony ankylosis), and Type B (with bony ankylosis). The lipping and spurring of the spine seen commonly with generalized osteoarthritis is not included in this grouping but it is included under the generalized disease of Group III. It should be clearly understood that this discussion is limited to what may be properly called primary spondylitis as manifested by a painful rigid spine. In reviewing the last three hundred patients seen with chronic arthritis, twenty-two cases of primary arthritis of the spine were found. Thus over 7 per cent of the total three hundred suffered from primary spondylitis. Of the twenty-two, ten were Type A (without bony ankylosis), and twelve were Type B (with bony ankylosis). These cases of spondylitis are briefly tabulated in tables 2 and 3.

Type A spondylitis, (table 2), is an unusual disease, or more probably an unrecognized syndrome, for we have found no description of this condition in the literature. Most remarkable is the observation that only males have been seen with this disease. The age of onset is in early adult life from seventeen to thirty. The duration of the disease has varied from one to sixteen years and has averaged six and nine-tenths years. All patients of this group are still alive and under periodical observation. The onset is insidious and gradually progresses to a poker spine. There is much pain and muscle spasm in the back. The patient walks with a peculiar waddle characteristic of a fixed spine and pelvis, exaggerated no doubt by adductor muscle spasm in the thighs. Dyspnea on exertion is the rule because of fixation of the rib cage. Chest expansion is often scarcely perceptible. The head is us-

TABLE II
SPONDYLITIS (TYPE A)

	R.C.R.	J.R.	C.B.S.	J.C.R.	W.N.J.	E.A.S.	R.W.	R.B.	H.F.*	I.H.*
Sex	M	M	M	M	M	M	M	M	M	M
Age	30	33	44	27	30	37	31	22	37	29
Age Onset	25	28	28	26	26	30	26	17	24	21
Onset, Ac. or Insid.	Insid.	Insid.	Insid.	Insid.	Insid.	Insid.	Insid.	Insid.	Insid.	Insid.
Const. Type	III	III	IV	IV	IV	II	III	III	IV	III
Gen. Health	Poor	Poor	Poor	Fair	Poor	Fair	Poor	Poor	Poor	Poor
Weight Loss	30	30	43	11	70	15	22	20	25	46
Joints Invol.	Spine	Spine	Spine	Spine	Spine	Spine	Spine	Spine	Spine	Spine
Rigid Spine	Yes	Yes	Yes	Yes	Yes	Mod.	Yes	Mod.	Yes	Yes
Deformity	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
B.P.	110/65	103/80	126/80	120/90	112/68	148/80	110/70	110/80	112/80	100/70
Foci	None	GB?	None	None	None	None	TB	None	None	None
Fever	None	None	None	None	None	None	None	None	Yes	None
LABORATORY: RBC & HB	N	N	N	N	N	N	N	N	Low	N
LABORATORY: WBC-Diff.	N	N	N	N	N	N	N	N	N	N
LABORATORY: Sed.-RBC	Rapid	Rapid	Rapid	Rapid	Rapid	Rapid	Rapid	N	Rapid	Rapid
LABORATORY: BMR	N	N	N	N	+25	N	N	N	N	N
X-Ray	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

*These two patients later developed acute polyarthritis without any change in the spine condition and with all manifestations of Group II Arthritis.

ually carried slightly forward and tends to produce a dorsal kyphosis with a loss of lumbar curvature. The constitutional type involved is the asthenic individual. The general health is poor and the patient shows evidence of a severe constitutional disease. Loss of weight is often marked, and in our series varies from fifteen to seventy pounds. The spine alone is usually involved, although muscle spasm in the back in most cases produces limitation of motion as well as pain in the shoulders and hips. In spite of evidences of severe constitutional disease with marked fatigue, loss of weight, and pain and stiffness in the spine, there is no fever, no anemia, no leukocytosis, and no obvious infectious foci in the majority of these patients. Most astonishing, however, is the absence of demonstrable roentgenologic changes in these completely stiff spines. One of this group has had the disease for nearly sixteen years, having much pain with rigidity of the spine, and as yet the spine shows no demonstrable bony ankylosis. All of the patients show an unusual roentgenologic appearance of the sacroiliac joints. There is loss of cartilage and presumably fusion. Very complete studies have been done on these patients but only a brief summary can be given here. These patients are alike as peas in a pod. No one can fail to recognize the picture when familiar with it. Patients who suffer from this disease are so identical in their many manifestations and so different from other types of arthritis that we have felt justified in considering Type A spondylitis as a separate disease syndrome.

Type B spondylitis (table 3) is characterized by stiffness of the spine associated with bony bridging between the vertebrae. The bridging may be local or generalized to include the entire spine. It may be associated with involvement of the hips and shoulders, and there is often ossification of the ligamentous attachments of muscles about the pelvis. The condition described by Knaggs as *Spondylitis Ligamentosa Ossificans* may be identical and the term is undoubtedly a good descriptive one for this group of cases. This striking picture must not be confused with the benign lipping and spurring so frequently seen in the spines of Group III Osteoarthritis. Type B spondylitis differs from Type A in several interesting respects, although the patients do not appear widely different on casual examination. Again, these patients are limited to the male sex. The average age and the age of onset are quite similar to the Type A cases. The character of the onset, however, is often acute, with a febrile illness, while the insidious onset is distinctive of Type A. The constitutional type, the general health, and the weight loss are not particularly different from Type A. Several of these Type B patients gave a history of one or more peripheral joints having been involved. Foci of infection are frequent in this group of patients and exceedingly rare in Type A. Attention must be called to the frequency with which tuberculosis occurs in the Type B group. Seven patients out of a total of twelve had presumptive tuberculosis. Fever is the rule in this group, while but one patient in the Type A group had fever and that only with occurrence of an acute infection.

TABLE III
SPONDYLITIS (TYPE B)

	J.G.	H.B.M.	W.J.M.	R.B.C.	M.O.	J.B.C.	O.R.	P.W.	F.E.D.	H.W.M.	H.M.L.	M.C.K.
Sex	M	M	M	M	M	M	M	M	M	M	M	M
Age	29	54	24	50	49	35	35	40	33	23	46	37
Age Onset	24	42	16	35	39	26	28	40	24	19	41	32
Onset, Acute or Insid.	Insid.	Insid.	Insid.	Acute	Insid.	Acute	Insid.	Acute	Insid.	Insid.	Acute	Insid.
Const. Type	III	IV	II	III	II	II	III	—	III	III	IV	II
Gen. Health	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor
Weight Loss	33	Slight	Slight	15	40	15	40	Yes	20	40	50	18
Joints Invol.	Spine Pelvis	Spine	Spine Pelvis	Spine Pelvis	Spine	Spine Pelvis	Spine	Spine	Spine Pelvis	Spine	Spine	Spine
Rigid Spine	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Deformity	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blood Press.	N	N	N	N	N	N	N	N	N	N	N	N
Foci	None	T.B.	None	T.B.	T.B.?	Several	T.B.	Pneumonia T.B.	T.B.	None	Empyema T.B.?	None
Fever	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No
RBC & HB	N	N	N	Low	N	Low	Low		Low	N	Low	N
WBC-Diff.	N	N	N	N	N	N	N		N	N	N	N
Sed.-RBC		Rapid	Rapid	Rapid	Rapid	Rapid	Rapid		Rapid			Rapid
X-Ray	Bridging	B	B	B	B	B	B	B	B	B	B	B

Anemia and leukocytosis occur more frequently in Type B than in Type A. However, the most startling difference between the two groups is in the roentgenologic findings. Type B shows massive bridging of the spine with calcification of ligaments, and many times this extends to the muscle attachments about the pelvis. The Type A patients reveal absolutely nothing to account for the rigidity of the spine.

To find twenty-two men with stiff, rigid, and painful spines among the three hundred routine chronic arthritics studied was something of a surprise. We have since gone over all the additional patients possible in search of a female with this disease, but up to the present time have not found one. This seems more significant, because of the three hundred arthritics studied more than half were women. The men of both groups were all afflicted in the prime of life, and nearly all of them had lived sheltered and protected from physical strain. Physicians, dentists, lawyers, and accountants were frequently victims. This spondylitis should not be confused with the condition ordinarily known as "laborer's spine". The pain and discomfort suffered by patients with Type A spondylitis is not unlike a severe and permanent lumbago, if one can imagine such an unhappy affliction. Coughing or sneezing may produce the most agonizing pain as well as marked intercostal muscle spasm. The Type B patients get much relief from pain when the ankylosis becomes complete and many of them reach an entirely painless stage in which their major discomfort is limitation of motion. Complete case reports, together with a discussion of etiology, treatment, and prognosis will appear shortly in a more detailed paper.

Summary

1. Two specific types of primary chronic spondylitis occurring only in males are reported,—one with bony bridging, and one without bony bridging. The twenty-two cases reported represent 7 per cent of the three hundred patients with chronic arthritis studied.

2. The Type A spondylitis without bony bridging is emphasized as being a clinical entity not usually recognized and about which little has been known. The surprising frequency of this condition warrants its consideration in the diagnosis of every young man with back pain.

3. A clinical grouping of chronic arthritis based upon similarity of clinical findings is given to present the relationship of spondylitis to this grouping.

The Teaching of Inheritance of Disease to Medical Students*

A Proposed Course in Medical Genetics

By Madge Thurlow Macklin, A.B., M.D., *London, Canada*

GENETICS has made greater strides in the last twenty-five years than any other of the biological sciences. So exact has this study become that the position of the ultimate determiner of hereditary characters is plotted on a chromosome map with the same exactitude with which the explorer denotes the geographical position of any given place on the earth's surface. With such an increase in knowledge, it is inevitable that an application of genetics to man should be made. Because it is much easier to trace the hereditary wanderings of some *peculiar* character through a human pedigree than it is to follow the trail of normal characters that are so common that they are universal, the study of human heredity has largely centered about pathological conditions.

This interest in pathological heredity has been enhanced to a certain extent by the fact that the brilliant work done in preventive medicine by the immunologists and sanitation experts has served to decrease very materially the death rate from infectious diseases. Persons spared from death by infection are kept alive to succumb to their constitutional disorders, so that we find the death rate from many of the degenerative disorders of the circulatory system, from cancer and from diabetes, rising. As many of these constitutional ills have an hereditary background, the triumphs of modern preventive medicine have served to throw into stronger relief the problems of human inheritance.

The medical profession as a whole has a very limited conception of how many diseases are inherited. It is true that many of them are rare, fortunately so, and that they do not bulk as large in numerical importance as do the infectious diseases, but being inherited they increase alarmingly as the years go by. From the standpoint of financial burden to the public, the whole public health program probably does not cost the people as much as do the hereditary diseases of the nervous system alone, with their schools for the feeble-minded, institutions for the insane, special schools for the blind and deaf, etc.

Premedical Training. The biologist who trains the medical student in his premedical days does much to stimulate interest and to instruct the student in the fundamentals of genetics. Unfortunately, however, most students

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are not able to see the value of this work, because the illustrations given them of necessity deal so largely with plant and animal life, usually animal life of a relatively low order. The information gained is thus apt to seem almost wholly dissociated from the realm of human disease, which is to be the practitioner's life work.

Even if the biologist were to give examples from pathological inheritance in man, the student is not yet sufficiently advanced to understand either the terminology or the significance of the illustrations used. One cannot make inheritance in Friedreich's ataxia mean anything to a student, when he has no idea of what Friedreich's ataxia is, what a knee jerk is, what claw foot is, etc. The student can absorb only so much at a time. The biology course should not include clinical subjects; it should give the student training in the fundamentals of genetics, so that when he comes to his clinical work the terms used in the discussion of inherited diseases may be intelligible to him.

Necessity for Medical Training in Genetics. The formal teaching of genetics should, however, not stop with the course in biology. Much knowledge concerning the inheritance of disease has been accumulating which is of very practical importance to the practitioner; practical because it will increase his diagnostic acumen, his therapeutic skill, his prognostic ability, and will at the same time enlarge his opportunities for preventive work. This knowledge, it is true, has not been taught to the medical student in the past, except as it came in as an aside in the clinical lectures of some clinician particularly interested in heredity. This lack of formal instruction in the past explains why many of our clinical teachers of today are not trained to bring the significance of heredity into their lectures. The students of today are receiving little information on the subject and as they become the clinical teachers of tomorrow, the lack of teaching in this branch will continue. For this reason we should have a definite course designed primarily to teach the student what is known of heredity in disease. It is true that not a great deal is known of some aspects of human inheritance, and that what we teach must be taught with many reservations. The same is true of many of the so-called facts of our medical knowledge of today. That does not deter us, however, from teaching what is known.

One of the greatest values accruing from the inclusion of such a course would be not so much the knowledge it gave to the particular students, as the knowledge they would ultimately give to us to correct our faulty notions and our incomplete observations. The student who is alive to the importance of heredity will observe and report accurately its manifestations in his patients. The student who never knew that diabetes and pernicious anemia were inherited will pass by the hereditary aspects of these diseases, because he will feel that it was by mere chance that several brothers and sisters were affected in one family. At a recent talk before physicians, I was astonished to find the numerous striking instances of inheritance of pathological conditions which even a group of only twenty-five men could recall from their practices. In some cases the knowledge

of the condition in other members of the family was of help in diagnosis. Thus they recalled a parent and two children with heart block; a man and his son operated upon for renal calculi; three generations of displaced lens; marked mental deficiency in mother and children; pernicious anemia running through several generations, etc. But none of these had ever crept into the clinical literature, because they had not seemed of sufficient importance. Yet we have those who are skeptical of the influence of heredity in disease, because there are so few published records of it.

I have said that a knowledge of inherited diseases would be of value from the diagnostic angle. It naturally follows that when the diagnosis is better, the therapeutic procedures that follow will be better and the results for the patient improved. Let me cite briefly two examples. So many relatively rare diseases come under the category of inherited diseases that, if they are not mentioned for their heredity value, the student may never hear of them. It is the rare disease that often gives the practitioner his chance to establish a reputation. For example, one roentgenologist advised removal of a child's arm for sarcoma of the humerus. The plate showed a growth, and sarcoma was the diagnosis. The family objected, and the child was sent elsewhere. The second physician showed not only a growth on the arm, but beginning growths elsewhere, and also similar bony excrescences in the father. A diagnosis of hereditary deforming chondrodysplasia was made and the child still has its arm.

A second child with very dry skin, sparse hair, and only one tooth was treated as a hypothyroid case and given thyroid extract. The patient was not benefited, and finally was taken to another physician, who recognized that the mother had very few teeth and diagnosed the cases of both mother and child as hereditary ectodermal dysplasia. The child showed more extensive involvement than the mother. He recognized the futility, even the cruelty, of thyroid treatment. Here was a child with no sweat glands, who was already handicapped in the endeavor to keep his body cool, being given medication which whipped up his metabolism and thus increased his discomfort.

One has only to think of pernicious anemia, and the opportunities there for preventive therapy with members of the family who have not yet shown the anemia but who are in the achylic and achlorhydric stage, to realize that a knowledge of the inheritance of disease is important from the point of view of preventive medicine.

It seems evident, that information concerning heredity in disease should not be given to students until they have had some lectures dealing with the diseases under discussion, and until they have become familiar with the signs and symptoms of disease. The proposed course which would give to the student a knowledge of heredity in pathological conditions will be of most value to him only if it is given in the final year, when he is acquainted with the subjects of medicine and surgery and all their branches. This does not mean, however, that inheritance is to be ignored in other courses and given to the student only at the

end of his career. The more widely trained our teachers become, the more they will correlate their courses with the course in medical genetics. The student will receive his biological background in his premedical days. When he enters upon his course in embryology, which deals with human development utilizing chick and pig material only for the early stages, he constantly meets with the influence of inheritance. Thus maturation of the ovum and sperm can be made a matter of great fascination by illustrating it with records of inherited human diseases, showing how through maturation comes the opportunity for segregation of characters which we see so strikingly illustrated in human pedigrees. Discussion of the mode of formation of the uriniferous tubule can be made a theme of thrilling interest, by the discussion of polycystic kidney and its inheritance. A dozen malformations of the developing fetus, which serve to emphasize the manner of normal development, can be made real to the student, not only by cooperation with the staff of the children's hospitals, whereby cases can be brought into class, but also by discussion of the inherited factors behind these conditions. I have found my students more than interested in embryology, through which runs a constant thread of heredity not only of the normal but of the abnormal characters.

In gross anatomy, an anomaly found in the dissecting room can form the basis of a short talk on what is known of the inheritance of that particular condition. In physiology the discussion of the mechanism of urine secretion and of the threshold of excretion for salts, sugar, etc., offers an opportunity for pointing out the hereditary factor in ortho-glycemic glycosuria. Pharmacology brings up hereditary peculiarities and idiosyncrasies to drugs. Biochemistry in teaching metabolism can point out the hereditary anomalies which allow certain persons to excrete alkapton, pentose, urobilin, or sugar.

In clinical fields, of course, opportunities are unbounded, and the value of a knowledge of inheritance to the physician who can thus get "diagnostic tips" is very real. The obstetrician who is having a hard time to deliver a woman whose pelvis is deformed through osteogenesis imperfecta and who has to resort to forceps in order to effect delivery may be able to save himself a suit for malpractice, if he brings into the world a baby with three or four fractures. Or if he has delivered a woman of one hydrocephalic child, he may be able to make the same diagnosis much more readily when the second shows the same defect, thus shortening the labor and modifying the technic employed to bring about birth.

The surgeon who is dealing with inguinal hernia, or with varicose veins, has opportunities for discussing the inheritance of these conditions. The pediatrician who has in clinic a baby with fatal jaundice can not only discourse upon the embryology of the formation of bile ducts, but upon the inheritance of that factor which inhibits the normal development of that minute part of the embryo, and so causes many babies in the same family to have the same disease. The neurologist has unlimited opportunities for

bringing out the inheritance factor in disease, and also for emphasizing the fact that knowledge of the presence of an inheritable disease in the family of the patient may be an aid to early diagnosis. Thus the mere diminution of a knee jerk, which might not be noticed ordinarily, becomes most significant when one knows that another member of the family had Friedreich's ataxia; or the enlarged limbs of a still healthy lad may assume a sinister meaning when we know that his older brother had pseudo-hypertrophic muscular dystrophy.

Thus all the way through the medical course the student would be learning of inheritance and of its importance in disease. Such instruction, however, would not remove the need of a course in medical genetics in the senior year. Such a course would round out the student's conceptions of the subject and would enable him to classify systematically the various manifestations of heredity as seen in clinical medicine. The senior student's clinical training would enable him to appreciate this course and to put the knowledge gained to use in his daily work. Even in such things as infectious diseases, he would learn that there are inherited immunities or partial immunities, so that the dark skinned races are less susceptible to skin infections and more susceptible to respiratory infections than are the light skinned races. He would learn that the children of one family respond to even the slightest irritant with a high fever, while in another family, the reaction is much less. He would see that some children have convulsions with a very low fever, while other children do not have convulsions even with a very high temperature. All such facts he will correlate with the great hereditary complex that goes to make up an individual.

With such a background our students may return to that conception from which modern methods have somewhat deflected us; namely, to the conception of the patient as an individual, not merely a case for the surgeon, the gastro-enterologist, or the gynecologist, but an entity whose physical, mental, and metabolic backgound contributes to his disorder. More than that, the physician with training in medical genetics will begin to take a long term view of medicine and its preventive and public health aspects. He will not neglect the patient, but he will visualize him as an entity in society. He will not only cure his present ill, if possible, but he will be able to forecast some that may occur to him because of his makeup, and to forestall them.

By Whom Should the Subject Be Taught? The subject should not, however, be left entirely to those who are teaching in the various branches of surgery or medicine, for not infrequently they are not familiar with or interested in the topic. We do not leave the subject of roentgenology to be taught as an aside by the surgeon, even though the latter constantly uses and refers to X-ray pictures as an aid to diagnosis. Similarly, medical genetics should be taught by a medically trained person who is thoroughly conversant not only with the subject of medicine but with the field of genetics, who knows it as intimately as the gastro-enterologist or the roentgenologist knows his special field of diagnosis and therapy.

Medical genetics is a specialty, only

in the same sense that pediatrics, internal medicine, or gynecology are specialties. It touches the work of the practitioner in many intimate ways; as he becomes familiar with it his usefulness to the patient and to the community is increased. Knowledge of medical genetics is far more essential to the practice of medicine than is the carrying out of many of the elaborate experiments in the preclinical years, which are designed for the research worker in that particular branch of science rather than for the medical student. It might be thought that since medical genetics is an essential part of general medical knowledge the teaching of it could be confined to the clinicians who give instruction in the symptomatology, the physical signs, the diagnosis and therapy of disease. The fact cannot be ignored, however, that clinicians do not usually take advantage of their opportunity to give instruction in the inheritance of disease and largely this is because of lack of familiarity with the subject. The data are scattered and often buried in inaccessible clinical reports and so are not available for the preparation of a clinic. The clinicians teach what they know, and leave untaught what is not familiar to them. Of course there are brilliant exceptions. I cannot forbear to mention Dr. Lewellys F. Barker who never misses an opportunity of discussing the heredity of the disease shown in his clinic if there be an inherited background. For the most part, however, it will be necessary that a person with medical training and with particular experience and training in the study of inheritance in disease should be the one selected to give the students instruction in this field.

It is true that the medical curriculum is over-crowded, but it was pointed out at a recent congress held at Edinburgh University, that the teaching of today is too largely permeated by the curative ideas of the medicine of yesterday rather than by the preventive ideas of medicine of today. It is in the field of prevention that medical genetics promises to be most useful. The meeting went on record as stating that the interest of the student was too largely directed to the end products of disease from the clinical angle, and to an unnecessary wealth of detail which had little or no bearing on his work as a practitioner on the preclinical side. The greatest need was for more applied biology (and what is more evidently applied biology than medical genetics) and also for more emphasis on prevention rather than on cure.

Opportune Time to Introduce Course in Medical Genetics. The time is ripe for the introduction of such a course into medical schools. The popularization of science by biology teachers and writers, the education of the public to some extent by physicians who are "heredity conscious", as well as by lectures, radio broadcasts and literature distributed by eugenic and genetic societies, are stimulating inquiries by the public which the physician must answer. If the medical schools do not recognize their opportunity and their obligation in this matter, the profession will be less well informed than is the laity. Medical courses should prepare the student for future needs; they should give him a background of

fundamentals on which he can erect a sound structure in later years. This is not being done with respect to inheritance in diseases. Although much is being published on this subject by those interested, it is not universally read, because the practitioner has not the necessary basic knowledge to enable him to grasp even the significance of many of the terms which are used.

It is true that at present there does not seem to be a great financial return from this particular study, and that therefore there will be need for the creation of endowed chairs in medical genetics, whereby research workers in this important field can not only teach medical students but can continue their investigations. As the profession and the public become alive to the possibilities, and as the latter learn to seek medical aid before the disease has started rather than after its onset, the physician will get his returns in the field of prevention rather than cure. Physicians are interested, and are becoming progressively more so, as they are learning more of the subject. One enlightened medical health officer, who is on a national Board of Examiners for medical licensure, regularly questions the candidates upon heredity in disease. He is keenly alive as to its public health aspects. The more general inclusion of such questions in State Board examinations would stimulate an interest in the subject. The matter of including in the Royal Society of Medicine in England a section which shall be devoted solely to reports of hereditary diseases is being advocated. The medical atmosphere is working toward the saturation point; there now must soon come a precipitation into an organized course of medical genetics designed to teach the student what is known of inheritance in disease.

Proposed Contents of Course

The following is a brief outline of a proposed course in Medical Genetics to be offered to students in their final year of medicine. The course would consist of thirty-six hours of lectures as a minimum and, depending upon the available clinical material in the hospital at the time, a certain amount of practical work. There would be much leeway here in the line the practical work would follow, just as there is variation in the choice of material for medical or surgical clinics.

The time table would be as follows:

2 hours. The fundamental concepts of inheritance, with special reference to the problems as met with in man.
2 hours. Heredity in endocrine diseases.
3 hours. Blood and blood vascular diseases in relation to heredity.
1 hour. Vasomotor and trophic disturbances.
1 hour. Genito-urinary disease.
2 hours. Digestive diseases and hereditary diseases of the spleen.
2 hours. Anomalies of metabolism.
3 hours. Eye diseases.
2 hours. Skin diseases.
2 hours. Skeletal diseases and malformations.
5 hours. Diseases of the nervous and neuro-muscular systems.
4 hours. Mental diseases.
3 hours. Tumors, benign and malignant.
1 hour. Miscellaneous conditions.

1 hour. Monstrosities and multiple births.

1 hour. Correct method of compiling family histories.

1 hour. Preventive and public health aspects of the problem.

Below are listed some of the conditions which would be discussed under each of the above headings.

1. Fundamental concepts of inheritance. Direct, indirect, sex-linked inheritance. Variations in mode of inheritance of disease in different families. Age factors in inherited disease.
2. Endocrine disturbances.
   Goiter, simple, exophthalmic; myxedema. Diabetes insipidus. Obesity. Adiposa dolorosa, Laurence-Biedl syndrome. Addison's disease. Diabetes mellitus. Miscellaneous endocrinopathies.
3. Blood and blood vascular system.
   Inheritance in blood groups, from medico-legal standpoint. Hemorrhagic diatheses including hemophilia, purpura hemorrhagica, and the great unclassified groups belonging to neither of the above. Telangiectasia, hemoptysis, hematuria, hematemesis. Pernicious anemia. Achylia gastrica. Sickle cell anemia. Polycythemia. Leukemia. Congenital defects of the heart. Hypertension, apoplexy, hypotension, angina pectoris. Varicose veins.
4. Vasomotor and trophic disorders.
   Urticaria, epidermolysis bullosa, angioneurotic edema, chronic edema, Raynaud's disease.
5. Genito-urinary diseases.
   Albuminuria of idiopathic origin. Polycystic kidneys. Bladder atony. Polymastia. Hermaphroditism. Hypospadias. Phimosis. Varicocele. Cryptorchidism, imperforate hymen, etc.
6. Digestive system. Liver and spleen.
   Gastric ulcer. Absent or malformed parts of digestive tract, such as salivary glands, atresia of esophagus, hypertrophic pyloric stenosis, imperforate anus, situs inversus, etc. Icterus neonatorum, acholuric jaundice, Gaucher's disease, cirrhosis of the liver, etc.
7. Anomalies of metabolism.
   Ortho-glycemic glycosuria, gout, alkaptonuria, cystinuria, pentosuria, steatorrhea, porphyrinuria, urobilinuria.
8. Eye diseases.
   Ptosis, ophthalmoplegia externa and interna, lagophthalmus, cryptophthalmus, blue sclerae, pterygium, megalocornea, microcornea, keratocornea, cornea plana, embryotoxon, corneal opacities not due to syphilis or tuberculosis, microphthalmus, anophthalmus, hydrophthalmus, glaucoma, defective or absent iris, cataract, ectopia lentis, color blindness, day blindness, night blindness, retinitis pigmentosa, amaurotic family idiocy, juvenile and adult forms of heredodegeneration of the macula, glioma retinae, optic atrophy, hypermetropia, myopia, nystagmus, astigmatism, strabismus.
9. Skin diseases.
   Anomalies of hair color, distribution, and absence of hair, teeth, sweat glands, etc. Dystrophies of the nails, of the teeth, of the skin. Tumors of the skin. Albinism, etc.
10. Skeletal malformations.
    The deformities of hand and foot, as polydactyly, brachydactyly, syndactyly, monodactyly, ankylosis, club foot and hand, contracture of fingers, fragilitas ossium, multiple cartilaginous exostoses, cranio-cleidodysostosis, oxycephaly, acrocephaly, achondroplasia, dwarfism, absent radii, cervical ribs, congenital dislocation of the hip, and numerous dystrophies of the bones and joints, cleft palate, hare lip.
11. Diseases of the nervous and neuromuscular systems.
    Progressive central muscular atrophy, Wernig-Hoffmann atrophy of infants, amyotrophic lateral sclerosis, hereditary spastic paraplegia, peroneal atrophy, Friedreich's ataxia, Marie's cerebellar ataxia, multiple sclerosis, extra-cortical axial aplasia, cerebral diplegia, Schilder's encephalitis, word blindness,

aphasia, paralysis agitans, hepato-lenticular degeneration, athetosis, facial paralysis, syringomyelia, myoclonus, periodic paralysis, tremor, neurofibromatosis, miscellaneous nervous disorders. Muscular diseases: muscular dystrophies, amyotonia congenita, myotonia atrophica, myotonia congenita.

12. Mental diseases.
Migraine, epilepsy, Huntington's chorea, microcephaly, mongoloid imbecility, macular degeneration, dementia praecox, manic depressive states, feeble-mindedness, etc.

13. Tumors.
All types of tumors of all organs, with evidence from the statistical standpoint as to the frequency of any given tumor in the population at large, and its significance in more than one member of the family.

14. Miscellaneous conditions.
Deaf mutism. Status lymphaticus. Allergic diseases. Hernia. Left handedness.

15. Multiple births. Monstrosities.
Twinning, anencephaly, spina bifida, hydrocephalus, hydropic kidney, etc.

16. Correct method of compiling family history with practical work.

In conclusion, let me again emphasize that, as we eliminate through our admirable public health organizations those diseases which are transmissible from person to person by means of infectious organisms and by filterable viruses, we are raising the percentage of the population who will fall victim to hereditary diseases. Some of these diseases may be of great importance only to the persons immediately concerned, and by the institution of preventive methods, these persons may have their lives still further prolonged for usefulness in the community. Many of the diseases, however, have a very direct public health aspect, since they are transmissible by germ plasm if not by organisms; they are of great economic importance to the public, since their victims require public aid in the maintenance of institutions, doctors and nurses to look after them. The only way to meet both problems is to have a medical profession trained and alert in the matter of human inheritance.

Editorial

THE USE OF LABORATORY PROCEDURES IN THE PRACTICE OF MEDICINE

Medicine has for centuries been so closely interwoven with the social relations of mankind that it is, and always must remain, a social function or profession; therefore, whatever affects people economically will also affect medicine. That such a statement is true, is amply borne out by the present depression of medical activities, and at the same time by the numerous studies and publications which are being constantly brought forward, all dealing more or less with the subject of the excessive cost of medical care, and all seeking a solution of a much unsettled and debatable problem.

Contemporary medicine has not yet been tempered with a proper degree of humility, and professional credulity—a benign form of unintentional dishonesty—has become a disease of very serious public menace. Specialists expound views, describe methods and allege cures, based far too much on impressions rather than facts. Specialism has made almost preposterous growth, and short-cuts to diagnosis, and extravagant methods of therapy are widely exploited. Credulity, as thus utilized in both diagnosis and treatment, has in part been responsible for some of the distrust in the medical profession among the rank and file of laymen, for admitted dissatisfaction within the ranks of the profession itself, and it has at least a bearing upon this problem of the so-called cost of medical care—a current subject of such heated discussion.

Excessive or improper reliance upon laboratory procedures has been conspicuous, particularly within recent years, and is believed by many to be one potent factor in the production of some of the practitioner's contemporary difficulties. Such a condition, if admitted, need not continue to exist.

There are perhaps four main varieties of laboratory methods or tests:

(a) Those of pure research.

(b) Those of presumed but unproved value. These have a legitimate field; their number will always be large and their diligent study is to be encouraged. From all of them a few will survive, as a result of accredited merit. Probably their clinical application should be studiously restricted to hospitals and teaching institutions, until their relative value, intrinsic sources of error or utter uselessness have been decisively demonstrated.

The alert practitioner and consulting internist should be informed about these two groups, though not actively concerned in their clinical application until their final status has been established.

(c) Those of established value, but of a complexity which puts their application beyond the range of the average individual, by reason of ex-

pensive equipment, the technic required or the time involved, or the infrequency of their need. In such a group one might mention basal metabolic rates, the Wassermann reaction, intricate clinical bacteriological studies, blood chemistry determinations, roentgen-rays and electrocardiographic tracings. Fortunately, the utilization of tests in this group is necessary in but a relatively limited number of cases. To use them intelligently, but three things are needed: An understanding of the physiological or pathological basis for the test; an unwillingness to interpret the results except in correlation with all the clinical data, critically judged by sound common sense; and first-hand information as to the methods used and care exercised in the laboratory in which the tests are made.

(d) Finally, those tests of long-tried and proved worth, simple, requiring a minimum amount of laboratory apparatus and a small expenditure of time, each capable of yielding diagnostic information which every physician should be able to interpret correctly. In this group might be included the simpler studies of the blood, urine, feces, gastric contents, spinal fluid and sputum. Years of teaching and observation corroborate Peabody's remarks that "in spite of the great contributions which the laboratory has made to clinical medicine, there has been surprisingly little change in the character or number of the technical methods that are essential to good practice. In spite of the extraordinary influence the laboratory has had on the development of medical science, as well as of medical education, there is as yet no cause for the physician to feel that he cannot keep up with the requirements of the best modern methods." The physician who cannot or does not judiciously utilize laboratory procedures is deficient in his clinical practice, and adds needlessly to the economic problems of the profession.

It would be utterly futile to argue against either the value or the usefulness of many laboratory methods which have been evolved in recent years. Yet in the excessive reliance upon, or in the unsound, non-discriminating use of, or the incompetent interpretation of laboratory tests, one can find a tremendous menace to modern medical efficiency; and so long as dogmatic reliance upon laboratory methods keeps reflective thinking and systematic observation subservient, poor clinical practice will continue.

The particular level to which an individual rises in terms of intellectual development depends upon the degree and consistency with which he exercises his many "mental muscles". The power of observation, the process of reasoning, the instincts of curiosity and wonder, keenness in special sense perception, are but so many intellectual muscles. They develop and expand by use; they wither and atrophy through disuse. Mental muscular development can be attained only through industry. This does not begin and end with the conscientious performance of the daily task. For those in the medical profession it means relentless study, inspired by a perennial, insistent demand for the solution of perplexities. Sustained mental development of this sort can be secured only by the exercise of hon-

esty, not merely in our dealings but in our thinking. Too few of us take the pains to study the origin of our cherished convictions. We are incredibly heedless in the formation of beliefs, and become filled with an illicit passion for them when any one proposes to rob us of their companionship. The world today needs sadly more of the intellectual freedom of the Greeks, the self-detachment and self-abnegating vigor of criticism so strikingly illustrated in the honest "know-nothingism" of Socrates.

SYDNEY R. MILLER.

Reviews

The Practitioner's Library of Medicine and Surgery. Supervising Editor, GEORGE BLUMER, M.A. (Yale), M.D., F.A.C.P.; David P. Smith, Clinical Professor of Medicine, Yale University School of Medicine; Consulting Physician to the New Haven Hospital. *Volume III: Practice of Medicine.* Associate Editor: HAROLD M. MARVIN, B.A., M.D., Assistant Clinical Professor of Medicine, Yale University School of Medicine. lii + 1400 pages, 44 illustrations. 1933. D. Appleton and Company, New York and London. Price, $10.00.

In the June, 1932, issue of the ANNALS, Volumes I and II of *The Practitioner's Library of Medicine and Surgery* were reviewed. These dealt, respectively, with Anatomy and Physiology as Applied to Practical Medicine and with The Technic of Physical and Laboratory Examination in Clinical Medicine. The entire set will consist of twelve volumes of which the last will be a composite index. Each volume is indexed separately as well. The present volume (III, *Practice of Medicine*) presents the material ordinarily covered in the standard textbook on internal medicine, with the exception of diseases of the nervous system. As compared to the texts of but a few years ago the changing emphasis on various diseases is apparent. Thus we find chapters devoted to Tularemia, Undulant Fever, Rat-Bite Fever, Psittacosis, Benzol Poisoning, and Agranulocytosis. Also there is added emphasis upon occupational hazards and industrial medicine in general.

To this volume there are 30 contributors. To list them all, with the subjects upon which they have written, would exceed the limits of this review. J. Burns Amberson provided the section on Tuberculosis; Alvin L. Barach, on Diseases of the Nose, Larynx, Bronchi, Lungs and Pleura; Arthur L. Bloomfield, on Streptococcal Infections; H. L. Bockus, on Diseases of the Liver, Gall-Bladder, Bile Ducts and Pancreas; Oswald E. Denney, on Leprosy; W. W. Duke, on Allergic Diseases; Raphael Isaacs, on The Anemias, Polycythemia, Leukemia, Lymphoblastoma, Agranulocytosis and Hemorrhagic Diseases; H. M. Marvin, on Diseases of the Heart and Diseases of the Blood Vascular System, and John H. Musser, on Typhoid Fever, Colon-Paratyphoid Infection, Tularemia, Influenza, Whooping Cough, Diphtheria, Tetanus, Anthrax and Glanders; to mention but a few of the authors.

As is inevitable with so many different authors, there is a marked difference in scale in the presentation of various topics. Throughout there is an evident desire to present the essentials. Some authors have done more; a few have, perhaps, fallen short of that goal. Generally speaking, those conditions which may be considered of minor importance have received even less attention than their position would seem to indicate. The short chapter of but one and one-half pages on Trichinosis may be taken as an example. As a matter of bookmaking it is to be questioned whether the many very short chapters should not have

been grouped; Chapter XXI, Micrococcus Catarrhalis Infections, has but 12 lines of text.

With but very few exceptions, the sections of this book are well written discussions of disease states. No one book can give exhaustive treatment to the constantly expanding field of internal medicine. The expert in a particular disease may find that in this book the extremely detailed information which has come to seem essential to him is lacking. Yet to the student and practitioner this volume can be fully recommended as presenting in a clear and attractive manner the necessary material for an understanding of the basic principles of the Practice of Medicine.

C. V. W.

Children's Tonsils In or Out. By ALBERT D. KAISER, M.D., xvii, plus 307 pages. J. B. Lippincott Company, Philadelphia, 1932. Price, $5.00.

This book, written as such a work should be by a pediatrician, is an interesting study and discussion of the relationship between pathologic processes in the tonsils and adenoids and general and local disease. It discusses the effects of tonsillectomy and adenoidectomy in prevention and treatment of about twenty different pathological states, not only those known to be associated with diseased tonsils, as rheumatic fever, glomerulonephritis, sore throat, etc., but also such indefinite and elusive conditions as malnutrition, anorexia, and mental retardation.

Most of the statistics are based on a ten-year study of 4,400 school children in Rochester, New York, the removal of whose tonsils was recommended. Half of the children of this group were operated upon; the other half, for various reasons, were not. The children were followed for ten years after tonsillectomy had been done or recommended, and the incidence of disease in both groups studied. For example, of the tonsillectomized group, 36 per cent had repeated attacks of sore throat before operation, and only 10 per cent had such attacks in the ten year period after operation. In the non-tonsillectomized group the figures showed a 41 per cent incidence of repeated sore throats before operation was recommended and a 35 per cent incidence in the following ten year period. The figures for the incidence of rheumatic fever are interesting; 2.3 per cent in the tonsillectomized group and 3.5 per cent in the controls, during the ten year period after operation was either recommended or done.

The lack of comparison of the observed statistics to those reported by other authors is noticeable. One also notes the absence of observation of the efficacy of tonsillectomy in preventing subacute bacterial endocarditis.

The section on anatomy, physiology and bacteriology of the tonsils is written by K. E. Birkhaug; that on the tonsils in communicable disease by W. L. Bradford; that on asthma and hay fever by S. S. Bullen. The indications for tonsillectomy in diabetes mellitus are discussed by G. B. F. Gibbs. A chapter on the surgical consideration of incomplete tonsillectomy and the significance of lymphoid hyperplasia is written by E. S. Ingersoll.

Children's Tonsils In or Out is interesting, easy to read, and the graphic charts can be analyzed at a glance. It is certain to be useful in spreading clearer understanding of the positive and the doubtful indications for tonsillectomy, and will certainly prevent many needless operations.

T. N. C.

Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System. By HARVEY CUSHING, 234 pages with 99 illustrations. Charles C. Thomas, Springfield, Ill., 1932. Price, $5.00.

The papers included in this volume had been delivered as lectures before prominent medical societies and published in current scientific periodicals. They "have been brought together for the convenience of those whom the general theme may interest". They include:

I. Neurohypophyseal Mechanisms from a Clinical Standpoint, the basis of the Lister Memorial Lecture, delivered at the Royal College of Surgeons of England, July 9, 1930.

II. Posterior-Pituitary Hormone and Parasympathetic Apparatus, basis of the William Henry Welch Lecture at Mount Sinai Hospital, New York, April 30, 1931.

III. The Basophil Adenomas of the Pituitary Body and their Clinical Manifestations (Pituitary Basophilism), basis of the Alpha Omega Alpha Lecture given at Yale University, February 24, 1932.

IV. Peptic Ulcer and the Interbrain, basis of the Balfour Lecture, given on Lister Day at the University of Toronto, April 8, 1931.

In these papers the author deals in a charming way with a fascinating field that is of fundamental importance to the general physician as well as to the neurologist, the endocrinologist, and the neurologic surgeon. The author has devoted much of his professional life and talents to the elucidation of the subjects herein discussed, and if there is a fault to be found in the discussion, perhaps it lies in the possibility that the smoothness of his attractive style may make this difficult, intricate, and controversial field seem too easy and too readily comprehensible. Some of his interpretations have been questioned by equally prominent workers in the same field and the author himself says in the preface, "Dealing as they do with somewhat novel topics—or at least with old topics from a renovated standpoint—it is quite probable that many of the interpretations are based on false premises and that even those which appear to be more securely grounded will not stand the test of time. This will make little difference, provided the papers help to draw attention to the long neglected interpeduncular region of the brain, unquestionably of fundamental importance to each of us, whatever may be his special field of medical work." Such situations are, of course, unavoidable in a rapidly changing scientific field.

Certainly there is no one better fitted by his own work and interests to present this subject to the profession, and the reader's pleasure will be enhanced by the literary excellence of the presentation and by the evidences of the author's scholarship.

T. P. S.

Asthma, Hay Fever and Related Disorders. A Guide for Patients. By SAMUEL M. FEINBERG, M.D., F.A.C.P., 124 pages, illustrated. Lea and Febiger, Philadelphia, 1933. Price, $1.50.

The conventional approach, used by the authors of most textbooks upon this subject, is used here. Starting with a historical review of the subject and working through such topics as complications, etiological agents, method of history taking, skin testing procedures, treatment, general care and advice, the book closes with a brief discussion of conditions which are less surely members of the specific sensitivity group of phenomena, although generally conceded as belonging in it, in some instances at least.

The author has limited his appeal strictly to the needs of the lay patient, avoiding the pitfalls inherent in any attempt to reach both patient and physician. Because of this, a dogmatic approach which materially aids in simplifying the subject for the uninitiated is permissible and is used with reasonable restraint.

The subject matter is handled in a clear and satisfactory manner, with the exception of an occasional tortuosity of expression that is not vital.

Certain phases of modern medicine are dependent upon concepts and considerations differing widely from those applying to medicine as a whole; it would seem that this was peculiarly true of manifestations of specific sensitivity. For that reason, a book of this sort should be of definite value as an aid in the clinical management of these cases.

H. M. B.

College News Notes

The executive office of the American College of Physicians will greatly appreciate information concerning any Fellows of the College who will be in Switzerland in August of the coming summer, at the time of the meeting of the International Goiter Conference in Berne.

Acknowledgement is made of the following gifts to the College Library of publications by members:

Dr. H. Sheridan Baketel (Fellow), Jersey City, N. J.—1 reprint;

Dr. W. R. Brooksher (Fellow), Fort Smith, Ark.—1 reprint;

Dr. Ralph O. Clock (Fellow), New York, N. Y.—2 reprints;

Dr. Ronald L. Hamilton (Fellow), Sayre, Pa.—1 reprint;

Dr. Maurice Kovnat (Associate), New Brighton, N. Y.—3 reprints;

Dr. Howard E. Marchbanks (Fellow), Pittsburg, Kansas—2 reprints;

Dr. Sydney Nussbaum (Associate), Brooklyn, N. Y.—8 reprints.

Dr. Harold F. Machlan (Fellow), was recently officially transferred from the Veterans Administration Hospital at Indianapolis to the hospital associated with the Veterans Administration Home, Dayton, Ohio.

Dr. S. A. Slater (Fellow), Worthington, Minn., was recently reappointed a member of the Minnesota Medical Executive Board. Dr. Slater is Superintendent of the Southwestern Minnesota Sanatorium, a member of the Board of Directors of the Minnesota Public Health Association and, during January of this year, was elected President of the Sioux Valley Medical Society.

Dr. David Riesman (Fellow), Philadelphia, Pa., has been elected Professor of the History of Medicine in the University of Pennsylvania to fill a newly established chair in this subject.

Dr. P. W. Rowland (Fellow), Professor of Pharmacology, University of Mississippi, was elected President-Elect for 1934-35 of the Mid-South Post Graduate Medical Assembly, at its recent meeting (49th) at Memphis, Tenn.

Dr. John A. Kolmer (Fellow), and Dr. Henry L. Bockus (Fellow), both of Philadelphia, Pa., under the auspices of the Medical Society of New Jersey, in coöperation with Rutgers University, recently delivered lectures on "Pneumonia Therapy" and "Diseases of the Liver", respectively, in connection with a series of graduate lectures for members of the Union County (N.J.) Medical Society.

Dr. John V. Smith (Fellow), Perth Amboy, N. J., has been appointed a member of the State Board of Institutions and Agencies.

Dr. Adolph Sachs (Fellow), Omaha, Nebr., has been elected Vice President of the newly organized Omaha Mid-West Clinical Society, the membership of which is limited to one hundred physicians.

Dr. Harlow Brooks (Fellow), New York City, has been named as an Adviser of the recently organized New York Institute of Clinical Oral Pathology. The initial membership is made up of one hundred physicians and dentists. It is announced that the activities of the organization will be extended over the country.

Dr. Karl E. Kassowitz (Fellow), Milwaukee, Wis., was recently elected President of the Milwaukee Pediatric Society.

Dr. Walter L. Bierring (Fellow), Des Moines, Iowa, was reëlected Secretary of the Federation of State Medical Boards of the United States at the Chicago meeting, February 13-14, 1933.

Dr. William D. Cutter (Fellow), Chicago, Ill., who is Secretary of the Council on Medical Education and Hospitals of the American Medical Association, was appointed Managing Editor of the *Federation Bulletin*.

Dr. Henry A. Rafsky (Fellow), has been appointed Consulting Gastro-Enterologist to the Rockaway Beach Hospital, New York City.

Dr. Charles H. McEnerney (Associate), Washington, D. C., was recently reëlected Secretary-Treasurer of the American Society for the Study of Arthritis; also Dr. McEnerney has been appointed as Consultant in Arthritis to the Providence Hospital, Washington, D.C.

Dr. David W. Kramer (Associate), Philadelphia, Pa., was recently promoted to Assistant Professor of Medicine at the Jefferson Medical College of Philadelphia.

ABSTRACT OF THE MINUTES OF THE MEETINGS OF THE BOARD OF REGENTS

Montreal, Canada
February 6-10, 1933

First Meeting, February 5

The Board of Regents of the American College of Physicians was presided over by Dr. F. M. Pottenger, President, Monrovia, Calif. The following members were present: Drs. Francis M. Pottenger, Maurice C. Pincoffs, George Morris Piersol, William D. Stroud, William Gerry Morgan, Walter L. Bierring, John H. Musser, O. H. Perry Pepper, James H. Means, James Alex. Miller, David P. Barr, Arthur R. Elliott, James B. Herrick, Clement R. Jones, Noble Wiley Jones, and W. Blair Stewart.

Dr. Carl V. Weller, retiring Editor of the ANNALS OF INTERNAL MEDICINE, was present on invitation. The Executive Secretary, E. R. Loveland, acted as Secretary of the meeting.

Abstracted Minutes of the previous meeting of the Board of Regents held at the College Headquarters, Philadelphia, November 13, 1932, were read and approved.

As incompleted business from the preceding meeting of the Board, the following resolutions were presented by Dr. William Gerry Morgan, Secretary-General.

DR. ELMER HENDRICKS FUNK

In an organization such as the American College of Physicians, with a restricted membership, the withdrawal of a single member by resignation or death is always an occasion for regret. In the death of Dr. Elmer Hendricks Funk the College sustains a loss greater than the mere withdrawal of one of its most influential members.

He was born in the City of Philadelphia and there he grew up and was educated, having received his medical education at Jefferson Medical College, from which he graduated with honor in 1908. He served there as resident physician, chief resident physician, medical director, and medical director and physician in charge in the department for diseases of the chest. He also served as resident physician in the Philadelphia Hospital for Contagious Disease and the Whitehaven Sanitarium for Tuberculosis. In all of these important posts he left behind him an enviable record for the highest type of medical efficiency as well as for his unfailing gentle courtesy and fair dealing.

Dr. Funk was blessed with the rare gift of winning the confidence, respect, and affection of those great leaders in medicine with whom he was fortunate enough to be thrown during the formative years of his professional career. These happy contacts contributed no little to the rapid strides which he early made in scientific medicine.

He had a prodigious capacity for work so that his days were filled with intensive study "investigation, research, teaching, writing, lecturing, work for organized medicine and civic philan-

thropy," all of the most dependable type and of the highest scientific value.

He contributed to many standard works and published in 1930 his volume entitled "The Diseases of the Respiratory Tract." He was recognized as an authority on the subject of tuberculosis.

On April 1, 1923, Dr. Funk was elected a Fellow of the American College of Physicians. At the San Francisco meeting in April 1932, he was unanimously elected Treasurer. His death occurred on May 13, 1932, before he had been able to undertake the arduous duties attached to that office. His death at the age of 46 prematurely cut short a career of great promise and has robbed the medical profession and the public of one of the most gifted men of his generation.

WHEREAS, Divine Providence has seen fit to remove from our midst through sudden and untimely death Dr. Elmer Hendricks Funk, who although among the younger Fellows was yet an earnest and energetic member and a physician of great promise; therefore be it

RESOLVED, That in his death the profession and the American College of Physicians has sustained an irreparable loss; and be it further

RESOLVED, That we extend to his bereaved family our deepest sympathy and send them a copy of these resolutions, and be it further

RESOLVED, That these resolutions be entered upon our records.

DR. JOHN ALDEN LICHTY

The name of John Alden Lichty is indelibly linked with the history of the development and progress of the American College of Physicians. Perhaps no single member has contributed more toward raising the College to its present enviable place among the outstanding medical organizations of the world. His untiring zeal and devotion to the best interests of the College is one of the bright pages in that history.

Dr. Lichty was born in Meyersdale, Pennsylvania, February 26, 1866. He graduated from Mount Union College, from which he received several degrees, and from the University of Pennsylvania School of Medicine in 1893, and from the University of Berlin in 1896. He occupied many important posts, among which may be mentioned Associate Professor of Medicine, University of Pittsburgh School of Medicine; visiting physician, Mercy Hospital, Pittsburgh; visiting physician, Columbia Hospital, Pittsburgh; consulting physician, Presbyterian Hospital, Pittsburgh; Superintendent of Clifton Springs Sanitarium, which position he occupied at the time of his death. He was a member of many of the leadng medical organizations of this country, and was past president of the American Gastro-Enterological Association. Dr. Lichty was a prolific writer, having published many splendid articles upon a variety of medical subjects. He contributed to several standard textbooks.

Dr. Lichty was elected a Fellow of the American College of Physicians on December 29, 1916. For many years he was a member of the Board of Regents, and for two years was third Vice-President. Of his many signal contributions to the College, perhaps the most notable was his organization of the Credentials Committee, of which he was the first Chairman, and on which he served with distinction.

In the death of Dr. Lichty on May 2, 1932, the College sustained an irreparable loss. Perhaps no single activity in Dr. Lichty's life was nearer to his heart and thoughts than were the affairs of the College.

WHEREAS, Almighty God in his wisdom has taken from among us Dr. John Alden Lichty, one of our oldest and most devoted members, who for more than forty years was a distinguished clinician; therefore be it

RESOLVED, That we enter upon our records this minute of our lasting regret at his passing, and our sincere appreciation of his long life of devotion to the best interests of his profession and of this College; and be it further

RESOLVED, That a copy of this report, preamble, and resolutions be sent to his bereaved family.

DR. CHARLES G. LUCAS

With the passing of Dr. Charles G. Lucas to his eternal rest July 7, 1932, the American College of Physicians has been deprived not only of one of its loyal members, but also of one of its strong, dependable guiding influences throughout nearly all of the years since it came into being.

Born in Cincinnati in 1868, Dr. Lucas received his education both premedical and medical in the institutions of Louisville, Kentucky. It was there that he carried on the practice of his profession. And during all those years was a member of the faculty of the Medical Department of the University of Louisville, in which in 1915 he was made Chief of the Department of Gastro-Enterology, a position he held until his death.

Dr. Lucas was a member of many of the leading medical organizations of the United States, among which was the American Gastro-Enterological Association, of which he was President in 1926; and the American College of Physicians, and served on the Board of Regents 1922-1923 and 1925-1928.

Few men in our profession enjoyed as wide a circle of devoted friends as did this outstanding physician. He will be keenly missed throughout the land wherever medical men foregather.

WHEREAS, By the inscrutable decree of Divine Providence the American College of Physicians has lost in the death of Dr. Charles G. Lucas one of its most esteemed members, who for many years took a leading and active part in the conduct of its affairs, as well as being an outstanding member of his profession; therefore be it

RESOLVED, That we enter upon our records this minute of our lasting regret at his passing and our sincere appreciation of his long life of devotion to the best interests of his profession and of this College; and be it further

RESOLVED, That a copy of this report, preamble, and resolutions be sent to his bereaved family.

Dr. Morgan further reported upon deaths of members during the past year, amounting to twenty-five Fellows and seven Associates; sixteen of these had been previously reported to the Board of Regents, the following being the additional list:

Fellows:

F. T. Billings, Pittsburgh, Pa., January 5, 1933.

Edward Bates Block, Atlanta, Ga., October 25, 1932.

Henry Daspit, New Orleans, La., December 19, 1932.

Gayfree Ellison, Norman, Okla., December 22, 1932.

William Engelbach, Springfield, Ill., November 22, 1932.

Edward Louis Heintz, Chicago, Ill., December 7, 1932.

Frank H. Pratten, London, Ont., December 10, 1932.

William Sydney Thayer, Baltimore, Md., December 10, 1932.

Carl Victor Vischer, Philadelphia, Pa., November 15, 1932.

Associates:

Alfred Henry, Indianapolis, Ind., December 12, 1932.

Fenton Benedict Turck, New York, N. Y., November 16, 1932.

Upon motion regularly moved, seconded and carried, it was

RESOLVED, that the report of the Secretary-General be accepted.

Dr. William D. Stroud, Treasurer, reported, in connection with incompleted business from the previous meeting, that in accordance with resolutions adopted by the Board of Regents, new bank accounts had been opened in the Royal Bank of Canada, Montreal, and the Provident Trust Company, Philadelphia; and that the securities belonging to the College had been transferred from Pittsburgh to the Girard Trust Company, Philadelphia.

The report of the Treasurer was received and placed on file.

In the absence of Dr. Sydney R. Miller, Chairman of the Committee on Constitution and By-Laws, the Executive Secretary presented his report. In accordance with instructions of the Board of Regents, the Committee on Constitution and By-Laws had published the recommended amendments to the By-Laws in the January Issue of the ANNALS OF INTERNAL MEDICINE. The amendments provide for:

(1) A consolidation of the Committee on Credentials, so that in the future there will be but one Committee for both Fellowship and Associateship. This Committee to be comprised of three members from the Board of Regents and three members from the Board of Governors;

(2) To provide that the Editor of the ANNALS OF INTERNAL MEDICINE shall be an ex-officio member of the Board of Regents.

The amendments were to be submitted at the General Business Meeting at Montreal on February 9. Upon motion regularly adopted, it was

RESOLVED, that the amendments, as presented by the Committee on Constitution and By-Laws, be approved.

Dr. George Morris Piersol, Chairman of the Committee on Credentials, presented the

following candidates, whose election to Fellowship was recommended:

Charles William Crankshaw, Consultant and Medical Advisor, Staff of the Medical Department-General, Prudential Life Insurance Company, Newark, N. J.;

Luis Manuel De Bayle, Nicaraguan Minister to the United States, Washington, D. C.;

Charles Austin Doan, Professor of Medicine, Ohio State University College of Medicine, Columbus, Ohio;

John B. Doyle, former Assistant Professor of Neurology, Graduate School of Medicine, University of Minnesota, and Neurologist to St. Vincent's Hospital, Hospital of the Good Samaritan and Queen of Angels Hospital, Los Angeles, Calif.;

Everett Colgate Jessup, Assistant Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, Roslyn, N. Y.;

Josephine Carrier Lawney, Dean and Professor of Medicine, Woman's Christian Medical College, Shanghai, China;

Malcolm Thomas MacEachern, Director of Hospital Activities, American College of Surgeons, Chicago, Ill.;

Thomas Turlay Mackie, F.R.C.P. & S., D.N.B., Instructor in Medicine, Columbia University College of Physicians and Surgeons, New York, N. Y.;

Harry A. Pattison, Director, Potts Memorial Hospital, Livingston, N. Y.;

George Alfred Skinner, Colonel, M.C., U. S. Army, Omaha, Nebr.;

Willard Burr Soper, Associate Professor of Medicine, Yale University School of Medicine; Medical Director, William Wirt Winchester Hospital, New Haven, Conn.;

Nathan Bristol Van Etten, Member, Committee on the Costs of Medical Care; Medical Director, Morrisania Hospital, New York, N. Y.

For Advancement from Associateship to Fellowship:

Arnold S. Anderson, St. Paul, Minn.
Ralph Lee Fisher, Detroit, Mich.
Michael Robert Haley, Dayton, Ohio.
Arthur Fisher Heyl, New Rochelle, N. Y.
John Francis Kenny, Pawtucket, R. I.
Erwin Curtis Miller, Worcester, Mass.
Frank B. Morrissey, St. Paul, Minn.
Rudolph Virchow Powell, St. Louis, Mo.
Benjamin Bruce Souster, St. Paul, Minn.
Edwin Chester Swift, Jacksonville, Fla.
Henry Hubert Turner, Oklahoma City, Okla.
J. Russell Twiss, New York, N. Y.

Upon motion by Dr. O. H. Perry Pepper, seconded by Dr. Arthur R. Elliott, and regularly carried, it was

RESOLVED, that the above list of physicians be and herewith is elected to Fellowship in the American College of Physicians.

Dr. Carl V. Weller, retiring Editor of the ANNALS OF INTERNAL MEDICINE, presented a report, reviewing his experience as Editor of the ANNALS and making suggestions and recommendations concerning the journal in the future. Among his comments, he mentioned the fact that 393 separate papers passed through the editorial office in the last nineteen months, indicating that there is an increased volume of material from which to select articles for publication in the journal, and, therefore, an added opportunity to improve the quality of the material selected for publication. In the past, it had been Dr. Weller's practice to devote approximately fifty per cent of the available space in the ANNALS to the papers delivered at the Clinical Sessions and fifty per cent to the papers selected from those submitted from at large for publication. In addition, it has been his aim to have the final article in each number represent the history of medicine, or ethical, or cultural aspects of medicine. He suggested the desirability of occasionally giving a comprehensive survey or review of some subject such as has not been done in the past. In regard to the size of the ANNALS, he recommended the present size of approximately one hundred and fifty pages per issue as desirable, but with effort expended upon the improvement of the quality of the journal; and he further recommended that the personality and individuality which the journal has achieved be maintained, and that changes in format and composition of material should be gradually

changed, if such changes are thought desirable. Dr. Weller has considered the ANNALS OF INTERNAL MEDICINE chiefly as a medium for postgraduate education in internal medicine. Its purpose was not to broadcast the more complicated pieces of work in experimental medicine, but to serve as the medium for postgraduate education to the more than three thousand subscribers scattered over the country.

On motion by Dr. Means, seconded and regularly carried, it was

RESOLVED, that the Board of Regents of the American College of Physicians extend to Dr. Carl V. Weller a vote of thanks for his very able conduct of the ANNALS OF INTERNAL MEDICINE since the death of Dr. Warthin.

The following resignations, after being individually considered, were by resolution accepted:

Fellows:
William P. Buffum, Providence, R. I.
A. H. W. Caulfeild, Toronto, Ont.
Clyde L. Cummer, Cleveland, Ohio.
Linton Gerdine, Athens, Ga.
H. Brooker Mills, Philadelphia, Pa.
A. W. Moody, Winnipeg, Man.
Walter B. Mount, Montclair, N. J.
Warren T. Vaughan, Richmond, Va.

Associates:
Edwin H. McIlvain, Philadelphia, Pa.
Henry J. Walton, Baltimore, Md.

Action on the resignation of the following was by resolution deferred:

Fellows:
I. Hope Alexander, Pittsburgh, Pa.
Thomas B. Futcher, Baltimore, Md.
Edward Livingston Hunt, New York, N. Y.

Associates:
R. W. Baer, Frederick, Md.
James W. Bruce, Louisville, Ky.
J. W. Earl Ellenberger, Wilkinsburg, Pa.
James J. Gable, Norman, Okla.
Charles A. Howland, Schenectady, N. Y.
Thaddeus Walker, Grosse Pointe, Mich.
Everett E. Watson, Salem, Va.

President Pottenger suggested that there were two matters that should receive some thought and be referred to the proper Committees. The first one concerns the question of the admission of new members to Associateship. The By-Laws provide that a candidate may be presented for Associateship after he has been graduated but three years, but this does not give the candidate sufficient time, in many cases, to be known by our Fellows in his locality, nor does it assure the College of the fact that he will remain in the field of internal medicine.

Dr. Pottenger, after some discussion by the members of the Board, suggested that possibly the Regent or the Governor in a given district might have a Committee of five or six Fellows appointed before whom candidates would come for a personal interview before their credentials would be referred to the Committee on Credentials.

The other matter President Pottenger wished to present was the suggestion of a change in our method for electing Life Members. He wished to refer to the Finance Committee for their consideration some plan by which members, so to speak, might underwrite their dues for the balance of their lives, and thus become Life Members. For instance, the maximum Life Membership Fee might be, as at present, $400.00, in addition to a Fellow's initiation fee. However, from the period of forty-five years of age to sixty-five years of age (when a member's dues may be waived), the member would need to pay only an amount equal to his dues for the intervening years. For instance, if a man is fifty years of age, he would pay his dues for fifteen years and become a Life Member, which would entitle him to active membership not only until sixty-five years of age, but for his entire lifetime. Many Fellows should be attracted to this plan of Life Membership who have not been attracted to the previous plan, requiring a total payment of $500.00. Dr. Pottenger further referred to findings established by skilled actuaries which show conclusively that life membership could be carried successfully and to the benefit of the organization initiating this plan.

Adjournment.

Second Meeting, February 7

The following members of the Board of Regents were present: Drs. F. M. Pottenger, George Morris Piersol, Maurice C. Pincoffs, Noble Wiley Jones, William D. Stroud, William Gerry Morgan, Walter L. Bierring, George E. Brown, John H. Musser, O. H. Perry Pepper, James S. McLester, Jonathan C. Meakins, James H. Means, James Alex. Miller, David P. Barr, Arthur R. Elliott, James B. Herrick, Clement R. Jones and Mr. E. R. Loveland, Executive Secretary.

Minutes of the previous meeting were abstracted and approved as read.

Dr. William Gerry Morgan, Secretary-General, presented several cases concerning fees and dues of individual members. Individual action is recorded in the official Minutes of the College. The following principles, however, were maintained: (1) the regular rules concerning annual dues as printed in the folder of the College should be maintained. This refers to the matter of $10.00 being the minimum to which the dues of full-time medical teachers and full-time employees of the State may be reduced; (2) former members who were dropped because of delinquency may be reinstated by the Board of Regents subject to the payment of all their delinquent dues; (3) the Board of Regents may waive partially, or fully, the dues of members who are physically incapacitated, but the waiver of said dues shall be made from year to year, subject to the recovery of the member and his again entering practice; (4) members shall not be required to pay dues after they have reached the age of sixty-five years, but the responsibility for notifying the Executive Offices shall be that of the member.

Upon motion regularly moved, seconded and carried, it was

RESOLVED, that the College donate to the John Crerar Library of Chicago the ANNALS OF INTERNAL MEDICINE, Volume VI, Nos. 1 to 6, inclusive.

Upon motion by Dr. McLester, seconded and regularly carried, it was

RESOLVED, that the Board of Regents approve of the action taken and the letters submitted by Drs. Pottenger and Morgan in connection with adding the influence of the American College of Physicians to the Medical Library Association for a reduction in the prices of German medical journals to subscribers in this country.

On behalf of the Chairman of the Board of Governors, Dr. W. Blair Stewart, who was absent, the Executive Secretary presented the following list of 112 candidates whom the Board of Governors had recommended to the Board of Regents for election to Associateship:

Edward Lee Alexander, Newport News, Va.
Francis William Baldwin, New York, N. Y.
Paul M. Bassel, Temple, Texas.
George C. Beach, Jr., Fort Sam Houston, Texas.
Orpheus J. Bizzozero, Waterbury, Conn.
LeRoy Walton Black, Rutherford, N. J.
James Lewis Blanton, Fairmont, W. Va.
Frank Runcorn Borden, Randolph Field, Texas.
James Albert Bradley, New Orleans, La.
Raymond W. Bradshaw, Oberlin, Ohio.
Timothy F. Brewer, Hartford, Conn.
Paul Brindley, Galveston, Texas.
Boyd Franklin Brown, Huntington, W. Va.
Harold F. Brown, Buffalo, N. Y.
Clyde Windom Brunson, Brooklyn, N. Y.
D. Grant Campbell, Montreal, Que.
Guy Walter Carlson, Appleton, Wis.
Douglas Gordon Chapman, Richmond, Va.
Charles Walter Clarke, New York, N. Y.
Thomas J. Coogan, Chicago, Ill.
Henry Charles Crossfield, East Orange, N. J.
Grover Cleveland Dale, Goldsboro, N. C.
Ward Darley, Jr., Denver, Colo.
Frank Lowell Dunn, Omaha, Nebr.
Edgar Durbin, Denver, Colo.
Philips J. Edson, Pasadena, Calif.
Ray Elledge, Hammond, Ind.
William White Falkener, Newport News, Va.
Ralph Manos Fellows, Galveston, Texas.
Clement Coleman Fenton, Morgantown, W. Va.
Carl Herman Gellenthien, Valmora, N. M.
Mark Gerstle, Jr., San Francisco, Calif.
George Albert Gray, Abilene, Texas.

Percival Allen Gray, Jr., Santa Barbara, Calif.
Edward Alfred Greco, Portland, Maine.
David S. Greenspun, Bridgeport, Conn.
Joseph Hajek, New York, N. Y.
Ronda Horton Hardin, Banners Elk, N.C.
Robert Ammiel Hare, Santa Barbara, Calif.
Benedict Richard Harris, Hamden, Conn.
Edward Hagerman Hashinger, Kansas City, Mo.
Michael Gerard Healy, Randolph Field, Texas.
Joseph Emmet Hirsh, Birmingham, Ala.
Roy Herbert Holmes, Muskegon, Mich.
D. Waldo Holt, Greensboro, N. C.
Arthur Hartt Jackson, Washington, Conn.
Guy Carleton Jarratt, Vicksburg, Miss.
Clarence Emory Johnson, Long Beach, Calif.
George Stephen Johnson, Denver, Colo.
Harry Gardner Johnson, Buffalo, N. Y.
Ernest L. Kiesel, Scranton, Pa.
John Glenwood Knauer, Washington, D.C.
Vincent W. Koch, Janesville, Wis.
Rudolph A. Kocher, Carmel, Calif.
Elmer Elgin Kottke, Des Moines, Iowa.
Manfred Kraemer, Newark, N. J.
Roderick Alexander Macaulay, Springfield, Mass.
Frank Rowe Maddison, Tacoma, Wash.
Bernard Abraham Manace, Corvallis, Ore.
Frank Raymond Mazzola, Jamaica, N. Y.
David William McKechnie, Montreal, Que.
Bernardine Thomas McMahon, Loomis, N. Y.
Joseph Marion Messick, Rochester, Minn.
Albert John Michels, East Liverpool, Ohio
Ida J. Mintzer, Jamaica, N. Y.
Edward Winfield Miskall, East Liverpool, Ohio.
Morris Eli Missal, Rochester, N. Y.
Daniel Murrah Molloy, Guatemala City, Guatemala
Allen Hoyt Moore, Doylestown, Pa.
Anita Mary Mühl, San Diego, Calif.
Frederick William Mulsow, Cedar Rapids, Iowa.
Jerome A. Murphy, Buffalo, N. Y.
Frederick W. Niehaus, Omaha, Nebr.
Edward Sterling Nichol, Miami, Fla.
Joseph Frederick Painton, Buffalo, N. Y.
George Washington Parson, Texarkana, Texas.
John Ryer Poppen, Washington, D. C.
Ernest Boring Porter, Coronado, Calif.
Harold Walter Potter, Newport News, Va.
Harry Hansell Preston, Hot Springs, Ark.
Robert McNair Purdie, Houston, Texas.
Warren Wilson Quillian, Coral Gables, Miami, Fla.
Jesse Dean Riley, State Sanitorium, Ark.
James O. Ritchey, Indianapolis, Ind.
Samuel Frederick Rosen, Savannah, Ga.
Max Harold Ruby, Waterbury, Conn.
Edwin Philip Russell, Rome, N. Y.
Robert Burns Sanderson, Crown Point, Ind.
Victor Ewald Schulze, Rochester, Minn.
Francis J. Scully, Hot Springs, Ark.
Harold Nathan Segall, Montreal, Que.
Laurence Fox Segar, Detroit, Mich.
Henry Kirven Speed, Sayre, Okla.
George Black Stericker, Springfield, Ill.
Landon Elwood Stubbs, Newport News, Va.
George Courtney Stucky, Lansing, Mich.
George B. Topmoeller, Cincinnati, Ohio.
Clarence Johnson Tidmarsh, Montreal, Que.
Neville Thompson Ussher, Santa Barbara, Calif.
Samuel A. Vogel, Buffalo, N. Y.
James C. Walsh, Watertown, N. Y.
Harold M. Walton, Loma Linda, Calif.
James Harold Watkins, Montgomery, Ala.
Francis Charles Weber, Newark, N. J.
Emil Weiss, Chicago, Ill.
William Graham Weston, Vicksburg, Miss.
James H. Wheeler, Henderson, N. C.
Joseph Wiener, Asbury Park, N. J.
Dwight Locke Wilbur, Rochester, Minn.
John Woodworth Wilce, Columbus, Ohio.
Ruth Walker Wilson, Beaver, Pa.
Burton L. Zohman, Brooklyn, N. Y.

The entire list was examined individually by members of the Board of Regents, after which the following resolution was adopted:

RESOLVED, that the above list of candidates shall be and are herewith elected to Associateship in the American College of Physicians.

The Executive Secretary presented mimeographed copies of the financial report of the College for 1932. The accounts of the College had been audited by an accountant and his detailed report was attached. Estimated income and expenditures for 1933 and suggested budgets were also presented. The reports were not discussed, but put in the hands of the Regents for examination and later analysis.

The Executive Secretary presented a list of forty-four names of members who were two or more years delinquent in their dues, and who, according to the By-Laws, are subject to being dropped from membership. The list had been presented to the Board of Governors and some of them expressed a desire to have a few weeks to go over it in a final effort to influence desirable members to retain their memberships and to make provision for the payment of their dues. It was pointed out that out of a total membership of more than twenty-eight hundred, this was a comparatively small list of delinquent members. On motion by Dr. Pepper, seconded and regularly carried, it was

RESOLVED, that the list of members delinquent for two or more years be referred to the individual Governors for the districts in which such delinquents reside, and if after a period of a month thereafter such delinquent members do not make arrangements for the payment of their dues, they may be dropped automatically from the rolls of the College.

Dr. James Alex. Miller, in the absence of Dr. Charles G. Jennings, Chairman, presented the report of the Committee on Public Relations as follows:

REPORT OF COMMITTEE ON PUBLIC RELATIONS

The final report of the Committee on the Costs of Medical Care is entitled: "Medical Care for the American People."

It is the twenty-eighth publication of a series representing an extensive and intensive effort to collect the factual data concerning numerous problems involved. These studies were made over a period of five years, after the expenditure of an extraordinary amount of thought, effort, and money.

The facts presented are of immense importance to the country as a whole and the medical profession in particular. They deserve the most careful study and consideration.

The detailed information is contained in the twenty-seven interim reports previously published, and only a brief summary is included in the final report. The main emphasis of the final report is placed upon certain definite recommendations proposed by the Committee as the basis for a plan of reorganization of medical practice, so as to meet the social and economic defects of the existing system brought out by the factual data.

These recommendations are in the form of separate majority and minority reports with a few members of the Committee declining to assent to either report.

The widespread discussion which has followed the publication of the final report is centered upon the recommendations suggested. This is most unfortunate as it has overshadowed the great value and significance of the studies upon which these recommendations are presumably based.

It is the opinion of your Committee that the publication of definite recommendations was premature and unjustified by the facts presented. A careful analysis of the text of the reports shows that the recommendations are really only tentative suggestions for future consideration and careful experimentation, and in our opinion should have been offered as such.

It is also our belief that the actual factual data contained in the various reports are of such value that they deserve most careful study on the part of the medical profession. These facts reveal a situation which calls for consideration and action leading to modification of existing medical practice, and in any such modification the medical profession should take a leading part.

It would be very unfortunate if prejudice caused by differences of opinion concerning the recommendations should belittle the value of the facts themselves. It would be still more unfortunate if either prejudice or inaction should deprive the medical profession of its rightful position of leadership in any program for remedying existing inequalities or injustices in the operation of the practice of preventive and curative medicine.

Our Committee, therefore, recommends that the individual Fellows of the American College of Physicians be urged to study the facts presented in the report of the Committee on the

Costs of Medical Care, uninfluenced by the acrimonious discussion which has been raised by the publication of the various recommendations, and we also recommend that the organized representatives of the medical profession in each community be urged to consider these problems in the light of their varying local needs and conditions, for it is our belief that by this method the enlightened leadership of the medical profession can point the way to improvements of great value, both to the public and to the medical profession itself.

In commenting upon the report, Dr. Miller said that the Regents might desire to have this report read at the General Business Meeting of the College and to have it published in the ANNALS OF INTERNAL MEDICINE. On motion recorded and regularly carried, it was

RESOLVED, that the Board of Regents of the American College of Physicians hereby approves the report of the Committee on Public Relations and directs that said report be printed in the ANNALS OF INTERNAL MEDICINE.

Dr. James B. Herrick re-presented the cordial invitation of the City of Chicago, as extended at the November meeting of the Board of Regents, for the College to meet in Chicago during 1934.

Adjournment.

Third Meeting, February 10

With Dr. George Morris Piersol presiding, as the new President, the meeting was attended by the following Regents: Drs. George Morris Piersol, Francis M. Pottenger, Maurice C. Pincoffs, William D. Stroud, William Gerry Morgan, Walter L. Bierring, John H. Musser, O. H. Perry Pepper, James S. McLester, Jonathan C. Meakins, James H. Means, James Alex. Miller, David P. Barr, Clement R. Jones, W. Blair Stewart, Luther F. Warren and Mr. E. R. Loveland, Executive Secretary.

Dr. Piersol introduced Dr. Luther F. Warren, of Brooklyn, newly elected member of the Board. The Executive Secretary acted as Secretary of the meeting.

By resolution, the Minutes of the previous meeting of the Board of Regents were dispensed with. The President called upon the Executive Secretary to present his report on the finances of the College, which follows. Mr. Loveland analyzed for the Board the comparative cost of conducting the last four Clinical Sessions and other details of the financial statements. He said in part: "When I submitted estimates of Income and Expenditures for 1932, one year ago, I estimated that the surplus for the year would be $9,970.00. The year's operation discloses a surplus of $9,623.08, or a difference of only $356.92. The total cash income for 1932 was $75,785.31, which is mentioned merely to apprise the Board of the volume of College business transacted. During the year 1932, $9,623.08 was added to the General Fund, making a total of $64,810.97; $975.00 was added to the Endowment Fund, making a total of $53,375.00. The combined funds now amount to $118,185.97.

" . . . . Increased expenditures for 1932 were occasioned by a far more expensive meeting, due to its being held in San Francisco and due to the awarding of the John Phillips Memorial Prize for the first time. While the ANNALS OF INTERNAL MEDICINE showed a deficit of $1,266.13 on Volume V, the journal showed a surplus for the calendar year of 1932 of $196.27. This improvement in the financial publication of the journal is due chiefly to the following: (a) a reduction in printing costs; (b) an increase, even under the present financial conditions, in the advertising income; (c) efficient and helpful coöperation of the Editor. A comparison of the advertising income in the past four years follows:

1929—$2,263.46
1930— 3,543.49
1931— 3,929.26
1932— 4,536.84

"Your Executive Secretary's office has been conducted as conservatively as possible, consistent with the business interests of the College. A reduction was secured in the rental of the College Headquarters, the extra budget for the Treasurer's office has been eliminated since the Treasury was transferred to Philadelphia, and one of the more highly paid secretarial assistants in the Executive Secretary's office was dispensed with on June 1, 1932. In the last

instance we may have erred, because the burden of work thrown upon the other assistants and the Executive Secretary has been so great in the preparation for this Session that all have frequently had to work late at night, Saturday afternoons and Sundays.

"During the year 1932, $4,077.82 has been invested, or reinvested, additionally in securities, bringing the total holdings up to $65,574.55. The cash balance on December 31, 1932, amounted to $48,285.55, of which $18,311.79 was on deposit in closed banks. During 1932, $8,892.54 was repaid by closed banks. The balance is carried on the books at its face value, due to the fact that the ex-Treasurer, Dr. Clement R. Jones, has assured the Board of Regents in the past that these balances will be paid in full.

"The budgets submitted for 1933 have been prepared as conservatively as possible by me. In view of the reduced income from Fellowship initiation fees occasioned by changed admission requirements, the reduction of Fellowship dues from $20.00 to $15.00 and of Associateship dues from $15.00 to $12.00, the reduction of Clinical Session guest fees from $15.00 to $12.00, the estimated surplus for 1933 is $5,142.50. The budgets provide for such economies as: a continued reduction in the office staff of the Executive Secretary, a reduction of 10 per cent in the Executive Secretary's salary, a reduction of 10 per cent in the Editor's salary, a reduction of $20.00 per month in the rental of the College headquarters, and all other savings that can reasonably be made."

Dr. Clement R. Jones, Chairman of the Finance Committee for 1932-1933, presented his report, recommending the following: (1) that remaining College accounts in closed banks in Pittsburgh be assigned by him as the former Treasurer to the "American College of Physicians"; (2) that the Board of Regents authorize the purchase of $5,000 in U. S. Bonds in addition to the $1,000 authorized at the meeting on November 13, for permanent investment; (3) the Committee recommends to the Board of Regents the reduction in the cost of Life Membership to $300.00, plus the initiation fee, up to the age of forty-five years. After forty-five years of age, the Life Membership fee shall be equivalent to the initiation fee plus the amount of dues from that age to sixty-five years of age. All Fellows now paying for Life Membership on the installment plan may come under this reduced amount; (4) the Committee recommends to the Board of Regents that the Editor's compensation shall be restored to $2,500 a year; (5) the Committee recommends to the Board of Regents the approval of the auditor's report and the financial accounts for the year 1932.

Dr. Pottenger commented upon the recommendation of the Committee in regard to Life Membership. He said that up to forty-five years of age, a member will pay his regular $300.00, plus the initiation fee; at forty-six, he would deduct from the $300.00 one year's dues; at forty-seven, two years' dues, and so on. He stated that the plan gives the member an opportunity of paying his Life Membership while he is productive, and expressed the hope that a great many members would desire to pay their memberships in full during the time their income is greatest, thus avoiding the burden the dues might be in later life. On the other hand, fees so paid will go into the permanent fund of the College.

Upon motion, seconded and regularly carried, the report of the Committee on Finance was accepted and the recommendations adopted.

Dr. W. Blair Stewart, a member of the Committee on Insignia, requested the Executive Secretary, Mr. Loveland, to read the report of the Chairman, Major Edgar Erskine Hume, who could not be present. The report was discussed freely and its recommendations were adopted in the following form:

> "(a) A cross of the shape of that of the Key of the College, approximately three inches in height, of green velvet or cloth to be worn at the option of the member on the right side of the academic gown to indicate Fellowship in the College;
>
> "(b) A similar cross of gold braid or cloth of gold would indicate Mastership in the College.
>
> "The use of cloth insignia of this type is in accordance with historical

precedent, and some of the gowns worn by continental University officials and others have such badges to indicate rank or special marks of merit. This plan has the advantage of being quite inexpensive, and as it is optional there should be no complaint by members of having to purchase insignia. On the other hand, if used by Fellows and others on commencement and other occasions, it will be a dignified means of indicating membership in this College. Moreover, if it is decided at some future time to adopt some special gown or hood, there would be practically no expense to making the change."

Upon motion made, seconded and regularly carried, it was

RESOLVED, that the Editor of the ANNALS OF INTERNAL MEDICINE and the Executive Secretary of the College, in conference with the Committee on Publications, be given the authority to change the printer of the ANNALS if they feel it desirable between now and the next meeting of the Board of Regents.

Dr. Stewart, Chairman of the Board of Governors, reported briefly on the work of the Board of Governors during the year, and of their meetings in Montreal. His report indicated that there has been a great deal of activity among the Governors in their individual communities and all are thoroughly interested in the work of the College. He reported to the Board of Regents that he, as Chairman of the Board of Governors, and by authority delegated to him by the Board, had appointed as members of the Committee on Credentials Dr. Egerton L. Crispin, Los Angeles, Calif., for a period of three years; Dr. Chas. H. Cocke, Asheville, N. C., for a period of two years; and Dr. Ernest B. Bradley, Lexington, Ky., for a period of one year.

The first matter under new business was the election of the Secretary-General and the Treasurer for the ensuing year. Dr. Clement R. Jones nominated the present incumbents, namely, William Gerry Morgan for Secretary-General and William D. Stroud for Treasurer, which nominations were regularly seconded. Dr. Musser moved the nominations be closed, said motion being seconded and carried. The Secretary, Mr. Loveland, was instructed to cast the ballot, and declared Dr. Morgan and Dr. Stroud regularly elected as Secretary-General and Treasurer, respectively, for the ensuing year.

In accordance with the provisions of the Constitution and By-Laws, the following Executive Committee for 1933-1934 was elected:

George Morris Piersol, Philadelphia, Pa., Chairman
Jonathan C. Meakins, Montreal, Que.
William Gerry Morgan, Washington, D.C.
William D. Stroud, Philadelphia, Pa.
Walter L. Bierring, Des Moines, Iowa
James H. Means, Boston, Mass.
James Alex. Miller, New York, N. Y.
Maurice C. Pincoffs, Baltimore, Md.
Francis M. Pottenger, Monrovia, Calif.

Upon motion by Dr. Pincoffs, seconded and regularly carried, it was

RESOLVED, that the American College of Physicians accept the invitation of the City of Chicago to hold its 1934 Clinical Session there.

Upon motion by Dr. Pincoffs, seconded and regularly carried, it was

RESOLVED, that Dr. James B. Herrick be appointed General Chairman of the 1934 Clinical Session, and that the exact date of the meeting and the headquarters be left to the General Chairman and the Executive Secretary.

President Piersol, in accordance with authority included in a resolution adopted by the Board of Regents on November 13, 1932, appointed the following standing Committee on Finance:

Charles F. Martin, Montreal, Que., Chairman (3 years)
James Alex. Miller, New York, N. Y. (2 years)
James S. McLester, Birmingham, Ala. (1 year)

President Piersol reported that there were certain other Committee appointments to be made, but with the approval of the Board, he would prefer deferring the appointments for some of these vacancies, until he had had an opportunity to consider the requirements more fully.

Adjournment.

ABSTRACT OF MINUTES OF THE MEETINGS OF THE BOARD OF GOVERNORS

Montreal, Canada

February 6-10, 1933

First Meeting, February 6

A regular meeting of the Board of Governors was held on the above date, and presided over by Dr. W. Blair Stewart, Chairman, with the following additional members present: Drs. Oliver C. Melson, Edward L. Tuohy, A. Comingo Griffith, Charles Hartwell Cocke, Clarence H. Beecher, J. Morrison Hutcheson, D. Sclater Lewis, Lewis B. Flinn, Edwin W. Gehring, Luther F. Warren, A. B. Brower, Charles T. Stone, Egerton L. Crispin, Henry F. Stoll, Samuel E. Munson, Thomas Tallman Holt, Adolph Sachs, Allen A. Jones, Leander A. Riely, Edward J. G. Beardsley, John O. Manier, Jabez Elliott, Charles Edward Riggs and Mr. E. R. Loveland, Executive Secretary.

The Executive Secretary, E. R. Loveland, acted as Secretary of the meeting, and read abstracted Minutes of the last meeting of the Board, which were approved as read.

He commented upon the application of the new rules for the admission of members, and asked Governors to investigate candidates fully and to write accordingly to the College Headquarters concerning each candidate. Dr. Stewart then reviewed the time requirements for Associates, namely, that a physician to be presented for Associateship must be a graduate of three years' standing, must not be younger than twenty-six years of age, and that after he has been elected an Associate, he becomes eligible for proposal for advancement to Fellowship at the end of three years, and must qualify for Fellowship within five years. At the end of that time, except by specific action of the Board of Regents, he will be automatically dropped from the rolls of the College. There followed some discussion as to whether or not twenty-six years of age is not too young, and whether three years after graduation is not too short a time for a man to be considered for Associateship. It was directly inferred that members of the Board of Governors should have this in mind when recommending younger men for election to Associateship, and that possibly only exceptional candidates should be considered at this early age.

Dr. Stewart also pointed out the effect of the new amendment to the By-Laws, which would consolidate the Committee on Credentials for Fellowship and the Committee on Credentials for Associateship; the new Committee to be composed of three members from each Board.

The Chairman further commented upon the list of elections to Fellowship by the Board of Regents, explaining that those elected directly to Fellowship were men of great prominence in various parts of the country, and outstanding men in the medical profession. They are physicians of mature years in professional work. All of their cases have been thoroughly investigated, and every one of them unanimously approved for election to Fellowship. The College is not interested in number of members, but in men of outstanding ability.

Chairman Stewart commented upon the clinical program prepared for the Montreal meeting, and expressed the opinion that the College owed the General Chairman, Dr. Meakins, a debt of gratitude for his work and that of his Committees. The President, Dr. Pottenger, also had prepared an outstanding program for the general sessions, and his work deserved the highest commendation. Dr. Stewart then expressed his appreciation and thanks to the Executive Secretary, Mr. Loveland, for his work. He said the Executive Secretary should not be considered an employee of the College, but as a man who has had the interests of the College at heart from the very moment he took his position, and whose work deserves outstanding recognition by all.

Chairman Stewart introduced President-Elect George Morris Piersol, who spoke briefly of the work of the Committee on Credentials, of which he had been Chairman for many years, and of the new Consolidated Committee which is planned to further facilitate and improve the work of selecting members in the future. He commended

the work of the various Governors and pointed out that they could be of even greater assistance by being firm in applying the requirements of the College to new candidates and by not forwarding to the College Headquarters any proposals but those which in their opinion merit election. He pointed out that the cost of investigating candidates varies from five to twelve dollars, depending upon the size of the community from which the proposal comes. This cost is made up chiefly from clerical service and postage, because letters or inquiry cards are addressed to every Fellow of the College in the community, or city, from which the proposal arises. Dr. Piersol further stated that present economic conditions have caused an increasing number of members to present their resignations, although the number coming into the College is much smaller than the average of other organizations. It is an appropriate function of the Governors to investigate such resignations, and not only to report upon them to the Executive Secretary, but to make an effort to retain desirable men in the College. Dr. Piersol then took occasion to say that the members were deeply indebted to the Executive Secretary for his work and for his coöperation in cutting down the expenses of the College.

At the request of Chairman Stewart, the Executive Secretary read a letter, expressing his regret at being unable to attend the meeting and conveying his regards to the Board, from Dr. Edward O. Otis, Governor for the State of New Hampshire, and dean of the Governors, being the oldest member.

Chairman Stewart introduced President Pottenger, who had just entered the meeting room. Dr. Pottenger spoke briefly of the importance of the Board of Governors in connection with their work in building the membership of the College and the selection of candidates. The Board of Governors should be an increasingly active body; it stands between the Board of Regents and the College membership; it fulfills the essential requirement of having a thoroughly active member representing every State and every Province. Dr. Pottenger reëmphasized the remarks made by President-Elect Piersol in regard to the application of the standards of admission.

Dr. Allen A. Jones, Chairman of the Committee on Credentials for Associateship, presented a list of sixty-four candidates whose credentials had been carefully reviewed by the College and deemed adequate for election to Associateship at a meeting of the Committee on November 13, 1932, at the College Headquarters, and another list of forty-eight candidates whose credentials had been reviewed on February 5 at Montreal.

Upon motion by Dr. Crispin, seconded by Dr. Griffith and regularly carried, it was

RESOLVED, that the complete list of 112 candidates be approved by the Board of Governors and recommended to the Board of Regents for election to Associateship. (The complete list appears in the Minutes of the Board of Regents as published on another page.)

The Executive Secretary presented a list of forty-four delinquent members of two or more years standing who were subject to being dropped from the rolls of the College. He asked individual members of the Board of Governors to look over the list for their particular districts and to be prepared to make recommendations in the course of the next month. In the meantime, the Board of Regents would be asked to delay action on the list, pending recommendations of the Board of Governors.

The Executive Secretary reported the death of twenty-five Fellows and seven Associates since the San Francisco Clinical Session.

The Executive Secretary reported upon action of the Board of Regents in connection with accepting and deferring various resignations. He distributed mimeographed copies of the financial reports of the College for 1932, and analyzed important features thereof.

On motion by Dr. Cocke, seconded and regularly carried, it was

RESOLVED, that it be the sense of the Board of Governors to express their appreciation to the Executive Secretary for his splendid work in this time of stress and for his efforts in maintaining such an excellent financial status as shown by the reports.

The Chairman opened the meeting for an open forum for discussion or comment by members of the Board.

Dr. Edward L. Tuohy, Governor for Minnesota, made the following inquiries: to what degree are the Associates in Minnesota qualifying for Fellowship under the three-year rule; does the College encourage membership among physicians engaged in border-line specialties, such as Pediatrics, Neurology and Roentgenology; should not the College concentrate more upon Internal Medicine; has the Board of Regents given any more attention to the matter of regional conferences with fewer annual meetings of the wider scope.

The Executive Secretary was asked to answer the first question. He pointed out that Associates who had been elected previous to 1929 were under no obligation to qualify for Fellowship, but those elected during 1929 and thereafter are required to qualify for Fellowship within five years. At the end of three years after election, an Associate is notified by the Executive Secretary that he is now eligible to be considered for Fellowship, and that he is expected to present the qualifications for Fellowship within two more years. In Minnesota, the majority of the Associates elected in 1929 have qualified for Fellowship. For the Committee on Credentials, Dr. Allen A. Jones expressed the opinion that Dr. Tuohy's second point was well taken, and that it should have further consideration. The Committee on Credentials have considered men engaged in the border-line specialties of Pediatrics, Neurology and Roentgenology eligible, provided they present proper credentials. It was pointed out that the General Chairman of each Clinical Session attempts to provide something in the Program for the men interested in the affiliated specialties, as well as Internal Medicine.

It was stated that there was a consensus of opinion that the present type of Annual Clinical Sessions would have greater value than regional conferences, but that the leading city would be alternated from one section of the country to another, in order that members in each region would have opportunities to attend the meetings periodically, if they could not travel longer distances every year.

Dr. Crispin opened a discussion concerning the minimum age for Associates, and expressed the opinion that most men at this age are not qualified for Associateship, and that they must be selected with considerable care. Dr. Crispin expressed the opinion that it is incumbent upon the Governors to handle these cases as best they can, but to have in mind the possibility of recommending a higher minimum age than at present provided.

Dr. Samuel E. Munson, Governor for Southern Illinois, made inquiry concerning how Governors shall report unfavorable action by the Committee to the candidates. Dr. Stewart suggested that this must be left to the individual judgment of the Governors. Dr. Cocke, of the Committee on Credentials, stated that approximately fifty per cent of the candidates proposed for Associateship are not immediately elected, but are put on a deferred list for additional data, seasoning, etc.

Adjournment.

Second Meeting, February 9, 12:30 p.m.

The second meeting of the Board of Governors was attended by the following, with Dr. W. Blair Stewart presiding: Drs. Oliver C. Melson, Edward L. Tuohy, A. Comingo Griffith, Charles Hartwell Cocke, J. Morrison Hutcheson, Edwin W. Gehring, Charles T. Stone, Egerton L. Crispin, Henry F. Stoll, Thomas Tallman Holt, Roger I. Lee, Adolph Sachs, Allen A. Jones, Leander A. Riely, Edward J. G. Beardsley, John O. Manier, Jabez Elliott, Charles Edward Riggs and the Executive Secretary, Mr. E. R. Loveland.

The Executive Secretary read an abstract of the Minutes of the previous meeting, which were approved as read.

The Executive Secretary reported that the complete list of candidates recommended by the Board of Governors had been regularly elected to Associateship by the Board of Regents; that the Board of Regents adopted a resolution providing that after the list of delinquent members presented at the previous meeting has been thoroughly

reviewed by members of the Board of Governors, which may be a period of a month or six weeks, such delinquents may be dropped, in accordance with provisions of the By-Laws, unless arrangements are satisfactorily made by which their delinquencies will be remedied.

At the direction of Chairman Stewart, the Executive Secretary read the report of the Committee on Public Relations, as approved by the Board of Regents.

Chairman Stewart declared an open forum for the discussion of any subject any member wished to present. He commented himself upon the matter of regional meetings. And this matter was discussed also by Dr. Tuohy, Dr. Cocke, Dr. Griffith, Dr. Roger Lee, Dr. Jabez Elliott and Dr. Crispin. Chairman Stewart summed up the remarks by stating that the matter of regional gatherings rests wholly with individual Governors, that the sentiments favor very largely the social type rather than the academic type of gathering.

Adjournment.

Third Meeting, February 9, 5:50 p.m.

The third meeting of the Board of Governors was held immediately after the General Business Meeting for the purpose of organization of the Board for the new year. The following members were present: Drs. Oliver C. Melson, Edward L. Tuohy, A. Comingo Griffith, W. Blair Stewart, Charles Hartwell Cocke, Clarence H. Beecher, J. Morrison Hutcheson, Edwin W. Gehring, Luther F. Warren, Charles T. Stone, Egerton L. Crispin, Henry F. Stoll, Samuel E. Munson, Thomas Tallman Holt, Roger I. Lee, Adolph Sachs, Allen A. Jones, Leander A. Riely, Edward J. G. Beardsley, Joseph Edward Knighton, Wallace Mason Yater, and Mr. E. R. Loveland, Executive Secretary.

The Executive Secretary, Mr. Loveland, acted as Secretary of the meeting, and Dr. W. Blair Stewart presided.

The terms of the Chairman and Vice-Chairman had expired with the Montreal Session, and following the election of new members of the Board of Governors, it became the duty at this meeting of the Board to elect a Chairman and Vice-Chairman for the succeeding period of three years. Dr. Stewart opened the meeting for nominations.

Dr. Egerton Crispin placed in nomination the name of Dr. W. Blair Stewart for reelection. Dr. Allen A. Jones and Dr. Cocke seconded the nomination, and Dr. Cocke moved that nominations be closed, and the Secretary instructed to cast the ballot. The latter motion was seconded and regularly carried.

The Executive Secretary cast the ballot for the unanimous reëlection of Dr. Stewart as Chairman for the ensuing term.

Members of the Board arose and applauded.

Dr. Stewart expressed his appreciation of the confidence the Board had reposed in him, and expressed the assurance that he would try to fulfill his duties to the best of his ability.

Nominations for the Vice-Chairman were opened, whereupon Dr. Adolph Sachs placed in nomination the name of Dr. Ernest B. Bradley for reëlection.

The nomination was regularly seconded, and upon motion nominations were closed and the Executive Secretary instructed to cast one ballot for the unanimous election of Dr. Bradley.

Upon motion by Dr. Samuel E. Munson, seconded and regularly carried, the Chairman of the Board of Governors was instructed to appoint three members to serve on the Committee on Credentials. Chairman Stewart stated he would announce his appointments in the near future.

Adjournment.

NOTE: At the end of the Clinical Session, Chairman Stewart announced the appointment of the following members to serve on the Committee on Credentials:

Egerton L. Crispin, Los Angeles, Calif. (3 years)

Charles Hartwell Cocke, Asheville, N. C. (2 years)

Ernest B. Bradley, Lexington, Ky. (1 year)

ABSTRACTED MINUTES—GENERAL BUSINESS MEETING of the AMERICAN COLLEGE OF PHYSICIANS

Montreal, Canada
February 9, 1933

The Annual General Business Meeting of the College convened at five o'clock in Windsor Hall, Montreal, with President Francis M. Pottenger presiding.

The Executive Secretary, E. R. Loveland, read an abstract of the Minutes of the previous meeting held in San Francisco, April 7, 1932, which was approved as read.

Dr. William Gerry Morgan, Secretary-General, was called upon and read the report of the Committee on Public Relations, as approved by the Board of Regents.

Dr. William D. Stroud, Treasurer, presented the following report for the year 1932:

"Upon assuming the office of Treasurer on July 1, 1932, the Treasurer's Office was transferred to the Central Office at 133-135 S. 36th Street, Philadelphia, and the major portion of the secretarial work has been carried on in that office, thus eliminating the extra budget for the Treasurer's Office, entailing a saving to the College of some $500 during the last half of 1932, and approximately $1000 a year in the future.

"The total cash income for the year 1932 was $75,785.31, with operating expenditures, including the unusually heavy expenses of the San Francisco Session, $66,162.23, leaving a surplus of $9,623.08, which has been added to the General Fund.

"On December 31, 1932, the Assets of the College were as follows:

General Fund	$64,810.97
Endowment Fund	53,375.00
Total	$118,185.97

Of this total, $65,574.55 is in securities on deposit in the Girard Trust Company of Philadelphia.

"$18,311.79 is still owing from the three banks in Pittsburgh which went into the hands of receivers in 1930 and 1931. $8,892.54 has been repaid by these banks during the year 1932. The cash balance on deposit in the Girard Trust Company of Philadelphia, the Provident Trust Company of Philadelphia, the First National Bank of Pittsburgh, and the Royal Bank of Canada was $48,285.55.

"There have been no defaults in interest by any of our securities during the year 1932, and such interest has totaled $2,906.43—considerably more than the Phillips Memorial Prize.

"At the November 13, 1932 meeting of the Board of Regents in Philadelphia, the Fellowship yearly dues were reduced from $20 to $15, and Associate dues from $15 to $12. Considering the times financially, the year 1932 has been definitely successful for the American College of Physicians. For this, much credit is due to the efficiency of the Executive Office and the Executive Secretary.

"Respectfully submitted,
William D. Stroud, M.D.,
Treasurer."

Upon motion seconded and regularly carried, the report of the Treasurer was accepted and placed on file.

The Executive Secretary, E. R. Loveland, presented his annual report. This covered some analysis of the financial report for the year, a report upon the financial side of the publication of the ANNALS OF INTERNAL MEDICINE, the cost of conducting the Annual Clinical Sessions, membership statistics, registration at the Montreal Session and the conduct of the Executive Offices.

Upon motion seconded and regularly carried, the report of the Executive Secretary was accepted and placed on file.

Dr. William Gerry Morgan, Secretary-General, was asked to present the report of the Committee on Constitution and By-Laws. He read the proposed amendments, Article by Article and Section by Section, as published in the January issue of the ANNALS OF INTERNAL MEDICINE.

On motion by Dr. O. H. Perry Pepper, seconded and regularly carried, the amendments were unanimously adopted.

President Pottenger expressed his pleasure at having been the President of the College for the past year and thanked the members of the organization for their coöperation and aid. He especially complimented the efficient organization of the Executive Offi-

ces of the College and the organization by Drs. Meakins and Martin of the Montreal Session. He then asked Dr. O. H. Perry Pepper and Dr. W. Blair Stewart to escort the new President, Dr. George Morris Piersol, to the platform.

In introducing Dr. Piersol, Dr. Pottenger said, "It is a happy occasion in one's life when his colleagues elect him to an office such as the Presidency of the American College of Physicians. It is an especially happy occasion at this time because our new President is a man who merits this position, not only because of his professional attainments, but also because of his devoted service to this organization. Dr. Piersol has been one of our hardest-working members. He has been ever thinking of this organization and looking after its interests. I present to you my successor, Dr. Piersol."

Members arose and applauded, after which Dr. Piersol assumed the chair. In his remarks, Dr. Piersol said in part, "Less than a year ago when you honored me by electing me to the head of this organization, I tried to express to you my appreciation and gratitude for that honor. I repeat it now. I am truly grateful to you for having conferred this distinction upon me and for the confidence and trust that you have indicated in me. I am not going to presume on your time now to try to make any sort of a formal address. My opportunity for that, I take it, will come next year. I do want to say, however, that in assuming this office, I do so with full realization of the responsibilities that go with it. I know that it will be a difficult task to live up to the record that has been established by our retiring President and his predecessors. I am hoping that the incoming administration, by reason of its interest and enthusiasm, will be able to accomplish the work in a meritorious way. In order that, during these rather difficult and uncertain times, we can continue to widen the sphere of influence of this organization and maintain its prestige, I earnestly bespeak the coöperation of all of you. Without that, no administration can succeed, but with that help and with the wise advice and counsel of the Board of Regents and the unfailing interest of the Board of Governors, it may be possible during this year to have an administration that will terminate its office one year hence in a successful manner. I want to thank you again and tell you how I am counting on all of you for help during the coming year."

Dr. E. J. G. Beardsley, in the absence of the Chairman of the Committee on Nominations, presented the following report:

"A meeting of the Nominating Committee was held at the office of the College in Philadelphia on the evening of November 12, 1932.

"The following nominations were made:

For President-Elect—Dr. J. C. Meakins, Montreal

For First Vice-President—Dr. C. G. Jennings, Detroit

For Second Vice-President—Dr. N. W. Jones, Portland

For Third Vice-President—Dr. J. H. Means, Boston

For Regents:
(*Terms expiring 1936*)
Dr. W. L. Bierring, Des Moines
Dr. J. H. Musser, New Orleans
Dr. O. H. P. Pepper, Philadelphia
Dr. F. M. Pottenger, Monrovia
Dr. L. F. Warren, Brooklyn

Terms expiring 1934 (to fill vacancy)
Dr. William J. Kerr, San Francisco

The following nominations were made for the Board of Governors:

For the term expiring in 1936:
Dr. Oliver C. Melson, Arkansas
Dr. Hans Lisser, Northern California
Dr. Tom Bentley Throckmorton, Iowa
Dr. Joseph Edward Knighton, Louisiana
Dr. James D. Bruce, Michigan
Dr. Edward L. Tuohy, Minnesota
Dr. A. Comingo Griffith, Missouri
Dr. Edward O. Otis, New Hampshire
Dr. D. Sclater Lewis, Quebec
Dr. W. Blair Stewart, New Jersey
Dr. Charles Hartwell Cocke, North Carolina
Dr. Julius G. Arnson, North Dakota
Dr. Alexander M. Burgess, Rhode Island
Dr. Robert Wilson, Jr., South Carolina
Dr. Clarence H. Beecher, Vermont
Dr. J. Morrison Hutcheson, Virginia

Dr. Frederick Epplen, Washington
Dr. John N. Simpson, West Virginia

For the term expiring in 1934:
to take Dr. Luther F. Warren's place—
Dr. Robert Anderson Cooke, New York

For the term expiring in 1935:
(to take the place of Dr. William Gerry Morgan, who has become Secretary-General—
Dr. Wallace Mason Yater, Washington, D. C.

On motion regularly made, seconded and unanimously carried, the report of the Nominating Committee was accepted and the Secretary-General instructed to cast one ballot for the election of all the candidates nominated. The Secretary-General, Dr. Morgan, announced the ballot had been cast, and the nominees elected.

Dr. O. H. Perry Pepper: "Mr. President, it is proper that we should at this meeting pass a vote of thanks to all the various agencies which have contributed to this very remarkably successful meeting. We should include in this vote of thanks the various institutions of Montreal, the various hospitals of the city, the Convention and Tourist Bureau, the press, and other local agencies. We should include especially the General Chairman, Dr. Meakins. Under Dr. Meakins' supervision there have been five or six Committees at work—the Committee on Arrangements, the Committee on Entertainment of Visiting Women (Chairman, Mrs. Meakins), the Committee on Transportation (Chairman, Dr. Kaufman), the Committee on Publicity (Drs. Sutherland and Benoit, joint Chairmen), the Committee on Convocation (Drs. Martin and Harwood, joint Chairmen). To all of these agencies and individuals Mr. President, I move you a rising vote of thanks by the College." The members arose and applauded.

President Piersol asked the President-Elect, Dr. J. C. Meakins, to come to the platform and make a few remarks.

Dr. Meakins: "Mr. President, Masters, Fellows of the American College of Physicians: I wish to express my few words in logical sequence to what has happened this afternoon. I must confess that I read pages of the ANNALS OF INTERNAL MEDICINE from a scientific point of view more than I do from the news point of view. I have been taught a very sharp lesson. It was just a week ago last night when our Executive Secretary, Mr. Loveland, was dining with me at my home that he informed me I had been nominated for President-Elect, and it had been published in the January issue of the ANNALS. I was, you may quite realize, tremendously surprised that you should have deemed me worthy of such an honor. I am probably one of the younger members of the College. I feel this confidence which you have placed in me imposes the serious obligation to fulfill your expectations. I have a long line of predecessors who have done noble work, and it is difficult to follow such a royal succession. But you may be assured, I will do everything in my power to maintain the dignity, to maintain the scientific and the professional standard of the College, which means so much to the medical profession of North America. I can only thank you sincerely for this honor which you have done me. I accept it with due humility.

"The organization here in Montreal, although there are only a few of us, are all loyal Fellows of the College. It was our desire to make this meeting as great a success as we could. My part in the matter was one as 'general', I suppose, and no general has yet ever won a campaign without brilliant staff officers. The success of this meeting depended upon the staff officers. For them I accept the vote of thanks, and I thank them as well myself. If it had not been for them, the whole organization would have been a miserable failure.

"I cannot let this opportunity pass without expressing my sincere thanks on behalf of myself and the local Committees to Dr. Pottenger for his unfailing kindness, consideration and courtesy to us. Furthermore, I want to make another expression, and that to Mr. Loveland. We were rather ignorant, true, as far as running this campaign was concerned, but his wise guidance, his almost uncanny penetration of our difficulties and what we should do, his clear letters, his unfailing and prompt consideration of us, made this possible.

"I think the American College of Physicians should be particularly thankful that they have such a capable Executive Secretary. It is only those who work with him who can fully appreciate that. I never appreciated it. I thought it was just an ordinary job. It is not; when one gets into the ramifications of it and sees the multitude of details which he puts before the local Committee, clearly and succinctly, one cannot help but offer him, on my behalf and on behalf of my committee, a very sincere vote of thanks."

All business scheduled to come before the Fellows and Masters of the College having been completed, adjournment followed.

AMERICAN COLLEGE OF PHYSICIANS, INC.
Balance Sheet, December 31, 1932

ASSETS

CASH:			
In Banks and on Hand		$30,173.76	
In Banks in Hands of Receivers			
Bank of Pittsburgh	$7,797.16		
Exchange National Bank, Pittsburgh	3,887.12		
Highland National Bank, Pittsburgh	6,627.51	18,311.79	$48,485.55
Accounts Receivable			539.11
Investments, as annexed			65,574.55
Accrued Interest on Investments			968.44
Inventory of Keys, Pledges and Frames			377.59
Deferred Expenses, 17th Annual Clinical Session (paid in advance)			2,242.61
Furniture and Equipment		$3,804.22	
Less allowance for Depreciation		1,604.39	2,199.83
			$120,387.68

LIABILITIES

Deferred Income:			
Advance Collections for Exhibits, 17th Annual Clinical Session		$1,880.94	
Advance Subscriptions for Volumes 7 and 8, Annals of Internal Medicine		320.77	2,201.71
			$118,185.97

FUNDS

Endowment Fund, as annexed		$53,375.00	
General Fund, as annexed		64,810.97	$118,185.97

GENERAL FUND, PRINCIPAL
For the year ended December 31, 1932

Balance, December 31, 1931			$57,166.71
Less:			
Transfer to Endowment Fund of Initiation Fees of Life Members paid prior to January 1, 1932		$ 100.00	
Award of John Phillips Memorial Prize and expenses of recipient incident thereto		1,878.82	1,978.82
			$55,187.89
Add:			
Net Income for the year, as annexed			9,623.08
Balance, December 31, 1932			$64,810.97

ENDOWMENT FUND PRINCIPAL
For the year ended December 31, 1932

Balance, December 31, 1931	$52,400.00
Life Membership Fees Collected During the Year Ended Dec. 31, 1932	975.00
Balance, December 31, 1932	$53,375.00

INCOME AND EXPENSES
For the Year ended December 31, 1932

INCOME

Annual Dues		$27,718.00	
Initiation Fees		10,275.00	
Interest on Bank Deposits		381.16	
Income from Endowment Fund	$2,365.79		
Income from Bonds Owned	540.64	2,906.43	
Profit from Sale of Keys, Pledges and Frames		148.54	
Collection and Exchange		241.67	
Receipts from Annals of Clinical Medicine		6.60	$41,677.40

EXPENSES

Sixteenth Annual Clinical Session			
Income:			
Exhibits	$4,609.73		
Guest Fees	875.00	$5,484.73	
Expenses:			
Salaries	$4,574.27		
Communications (Postage, Telephone, Etc.)	646.47		
Stationery and Office Supplies	83.55		
Printing	1,927.90		
Traveling Expenses	8,876.00		
Entertainment	286.65		
Advertising	323.00		
Reporting	166.25		
Badges	297.09		
Ladies Committee	98.90		
Publicity	180.83		
Banquet	75.85		
Miscellaneous	557.40	18,094.16	
Net Expenses		$12,609.43	
Annals of Internal Medicine			
Income:			
Subscriptions			
Volume I	$ 23.65		
II	6.04		
III	62.25		
IV	44.58		
V	590.17		
VI	17,335.44		
Advertising			
Volume V	2,359.87		
VI	2,176.97		
	$22,598.97		
Expenses:			
Salaries	$5,226.92		
Communications (postage, telephone, etc.)	1,149.64		
Printing	15,840.64		
Traveling Expenses	53.13		
Stationery and Office Supplies	3.34		
Miscellaneous	129.03	22,402.70	
Net Income	$ 196.27		196.27
Forward		$12,609.43	$41,873.67

Forward		$12,609.43	$41,873.67
Executive Secretary's Office			
Expenses:			
Salaries	$9,219.31		
Communications (postage, telephone, etc.)	1,085.20		
Stationery and Office Supplies	419.35		
Printing	501.03		
Rent and Maintenance	2,980.84		
Traveling Expenses	2,812.05		
Annual Audit	150.00		
Premium on Surety Bond	20.00		
Miscellaneous	111.24		
		17,299.02	
Treasurer's Office			
Expenses:			
Salaries	$240.00		
Communications (Postage, Telephone, etc.)	59.50		
Stationery and Office Supplies	4.13		
Printing	2.90		
Traveling Expenses	492.30		
Annual Audit	50.00		
Premium on Surety Bond	153.50		
Fee for Storage of Securities	75.00		
Miscellaneous	10.00	1,087.33	
Annals of Internal Medicine Distributed Free to Life Members		144.00	
1932-33 Directory (Cost of Production and Distribution of Supplement)		727.19	
Depreciation on Furniture and Equipment		380.42	
Loss on Equipment Traded In		3.20	32,250.59
Net Income for the Year Ended Dec. 31, 1932			$9,623.08

INVESTMENTS
December 31, 1932

Par Value	Bonds	Cost
1,000	Borough of Steelton, Pa., Paving, 4½s, Jan. 15, 1933	
1,000	Borough of Steelton, Pa., Water Improvement, 4½s, Jan. 15, 1933	$ 3,071.25
1,000	Borough of Steelton, Pa., Fire Apparatus, 4½s, Jan. 15, 1933	
4,000	Canadian National Railway, 4½s, 1956	3,930.00
5,000	Canadian National Railway, 5s, July 1, 1969	7,042.50
2,000	Canadian National Railway, 5s, Oct. 1, 1969	
2,000	Canadian National (West Indies) SS. Co., 5s, 1955	2,040.00
2,000	City of Covington, Ky., 4¾s, 1946	2,134.01
2,000	City of Detroit, Mich., Lighting, 4¼s, 1944	2,010.40
2,000	City of Detroit, Mich., Street Ry., 4¼s, 1949	2,025.26
2,000	City of Houston, Texas, School District, 4¾s, 1942	2,077.50
2,000	City of Los Angeles, Calif., Sewage Disposal "B", 5s, 1943	2,158.24
1,000	City of Montreal, Canada, 5s, 1956	1,071.30
2,000	City of Newark, N. J., Series 2, 4½s, 1944	2,075.00
10,000	City of Philadelphia, Pa., 4½s, 1949-79	10,225.00
2,000	City and County of San Francisco, Calif., Fire Protection, 5s, 1941	2,137.12
2,000	City of Seattle, Wash., Light & Power, 4¾s, 1957	1,995.00
2,000	City of Toronto, Canada, Local Improvement, deb. 5s, 1936	2,020.00
500	Oklahoma Gas & Electric Co., deb. 6s, Series A, 1940	487.50
2,000	Borough of N. Y. Authority, Interstate Bridge Bond, Series B, 4½s, 1952	2,042.20
2,000	Port of New York Authority, Interstate Tunnel, Series E, 4¼s, 1958	2,065.40
2,000	Province of Alberta, Canada, deb. 4½s, 1956	1,896.00
5,000	Province of Ontario, Canada, deb. 4½s, 1933	4,925.79
2,000	Province of Ontario, Canada, deb. 4½s, 1942	2,015.00
1,000	Province of Ontario, Canada, deb. 5s, 1942	1,052.26
2,000	U. S. Treasury, 4s, 1954	1,998.13
3,000	U. S. 4th Liberty Loan, 4¼s, 1938	3,079.69
64,500	Total (Annual Yield, 4.4322%)	$65,574.55